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JOURNAL OF GERONTOLOGY

Volume 1 OCTOBER, 1946 Number 4, Part 1

The Dawn of Gerontology

FRANK HINMAN

POPULATION EXPERTS SAY THAT BY THE TURN OF THE CENTURY THE MEDIAN AGE IN THE UNITED STATES WILL BE CLOSE TO 50 YEARS INSTEAD OF THE PRESENT 30. MAN HAS DEFIED NATURE'S DOCTRINE OF THE SURVIVAL OF THE FITTEST AND YET HAS DONE NOTHING ABOUT IMPROVING THE RACE THROUGH EUGENICS. MAN'S HOPE FOR SURVIVING SUCH INFRINGEMENT OF BIOLOGIC RULES LIES IN HIS BRAIN. SINCE MENTAL ABILITY REACHES ITS PEAK AROUND THE AGE OF 60, THE INCREASE IN THE NUMBER OF OLDER PEOPLE CAN AID FUNDAMENTALLY IN SAVING THE RACE FROM EXTINCTION. TILL NOW, LITTLE HAS BEEN DONE TO USE OR TO IMPROVE THE INTELLECT AND MATURE JUDGMENT OF ELDERS. THE SCIENTIFIC STUDY OF ALL PHASES OF AGING —GERONTOLOGY—HAS ONLY BEGUN, AND HAS THE IMPORTANT TASK OF SALVAGING INTELLECT AT A TIME WHEN SOCIETY NEEDS IT MOST.

HE LOOKED it when he said, more to himself than to anyone in particular, as he took his seat for lunch, "I'm through, I'm finished," adding in answer to questioning glances, "I have retired." A man of 65 with nothing wrong physically faced a future of many years for which he had made no plans. Over night the executive position to which he had worked up had slipped out of his hands for no other reason than his age. What would he do?

Elders at present find few opportunities in industry. Professional men are about the only ones who can ease off in later years. It is odd but true that those whose job has been manual make the adjustment of retirement more smoothly than those whose work has been mental. Given a small pension, manual workers are content to putter around the house, do a little gardening and live from day to day with no thought of the future. Those higher up in the educational scale, however, are terribly bored with nothing to do. The day laborer can keep busy with his puttering and gardening, but to most white collar pensioners this would be deadly and lead almost certainly to some physical or mental disaster. To the white collar worker, puttering and gardening are too lonesome and aimless. Every healthy elder needs an outlet in order to round out a full, contented life, and this outlet not only must be of interest but must at least appear to be worthwhile. If gardening is of value and the elder likes to garden, then it will be a proper outlet.

Why the present concern? it may be asked. Haven't the aged always retired when they reached the point either of inaptitude or of chronologic necessity? Of course, but the significance of retirement has been changed completely by the overwhelming increase in the number of people who now reach the age of retirement.

The first reliable estimate of the population of the world was not made till the beginning of the seventeenth century, at which time 445,000,000 was a good guess (1). Authentic sources in 1937 placed the total population close to 2,104,000,000. In three hundred years the human species increased in numbers more than fivefold. New worlds to conquer and the mechanical

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revolution will explain this remarkable increase. The factors which lead to an increase or decrease of population, however, are not always clear. The population of India, for example, in spite of the fact that three of every four children die before reaching two years of age and that there is a very high subsequent death rate, increased by 50 million from 1930 to 1940. The population of the United States, largely through immigration, doubled every twenty-five years during the nineteenth century, but with a diminishing birth rate and restricted immigration, there has been a bare increase of 7 per cent in the last decade. In 1930, the population was 131,000,000. Today it is well over 140,000,000. Had the earlier rate of growth continued, the year 2000 would have seen more than 600,000,000 people in the United States. Whelpton (2), assuming no immigration, a decline in the birth rate, and an increase in longevity, computes a "maximum of nearly 154,000,000 in 1985 or thereabouts, after which it will begin to decline . . . and by the end of the century our numbers will be little, if any, greater than in 1920." It would seem, therefore, that the population of this country soon will become stationary at somewhere between 100 and 150 million people and, to quote the same authority, "it can be shown quite conclusively that the smaller number would be best from an economic standpoint." Are we then already overpopulated for the optimum of individual welfare?

When Marcus Aurelius wrote his *Meditations*, each individual born into the Roman empire lived an average of 23 years, and seventeen centuries later even in the United States life expectancy at birth was only 40 years (table 1). It was 47 years in 1900, but it was 60 years in 1930. In three decades the expectancy of life increased more than half the average life time of the Roman. Today every child born in this country has an expectancy of more than 64 years, and when the maximum of population is reached in 1985 or thereabouts, the average lease on life probably will be over 70 years—three times that of the Roman (3). From 1930 to 1940 the population increased 7.2 per cent, but the proportion of people over 65 increased 35 per cent in the same decade—almost five times the general increase. By the turn of the century, so population experts say, 32 per cent of the population will be elders over 54, and only 23 per cent, youth under 20 (table 2). Suppose that by the year 2000 there is an optimum population of 100 million with little change in the social structure: 45 million adults will be supporting 55 million dependents. Instead of a median age of around 30 as at present while youth still

TABLE 1. LIFE EXPECTANCY AT BIRTH (3)

In Roman Empire 27 B.C. to		In United States				(estimated)	
395 A.D.	1850	1900	1930	1940	1945	1980	2000
23	40	47	60	63	65	70	70+
(an increase of 17 years in 19 centuries)		(an increase of 20 years in half a century)					

outnumbers the aged two to one, the median age fifty-five years hence will be close to 50 and youth will be far outnumbered. The United States will then be truly a country of elders.

None of the youth has the right to vote, but all of the elders, even the nonagenarians and centenarians, except those few legally declared incompetent, retain the full right of suffrage. Has this fact no significance in a democracy? Some of the causes of these changes should be considered.

Almost everyone nowadays is biologically minded enough to believe that man is an animal descended from lower forms of life through the natural laws of evolution. Only a few persons, however, will admit that these laws are still in force and apply to man's social and human functions as well as to his biologic function as an animal in the past. Mutations and natural selection are as active in human behavior and relations, in the government of nations, and in international disputes as in any survival of the fittest in the long struggle for animal existence. What makes man differ from other animals is his code of human values, which values have struggled through the changes of past history and now face the struggle of existence through the mutations and selections of the future. However, future changes in human values need not be left to chance as were the physical changes in biology, because man himself and not nature is their trustee. The United Nations Organization by its promise of mutual satisfactions is a product of evolution in human values and faces the struggle of survival.

The care of the sick, the helpless, the needy, and the insane has long been recognized as purely human. For the sake of humanity man has shouldered a tremendous burden of social obligations, and as yet he is barely conscious of these new qualities which make him human. By nature he is not altruistic, and he will become so only if the changes and survivals of human values choose this route. Just as ethics has evolved from the long struggle of the human conscience through gladness for right, sadness for wrong (*Ethicogenesis* of Leake, 4), so will human values evolve into still greater values only by reason of greater mutual satisfactions. As Huxley puts it (5): "The future of progressive evolution is the future of man. The future of man, if it is to be progress and not merely a standstill or a degeneration, must be guided by a deliberate purpose." Ob-

TABLE 2. PERCENTAGE BY AGE OF THE POPULATION OF THE UNITED STATES (1, 3)

	1900	1930	1940	1945	1980 (estimated)	2000 (estimated)
0–19 (Infancy—Adolescence)			34.5	33.0 (46 million)	25.8	23.0
19–54 (Adulthood—Maturity)	(only 17% over 45)		50.7 (26.5% over 45)	49.0 (69 million)	47.0	45.0
54–64 (Climacteric—Later Maturity)			8.0	9.0 (12 million)	12.8	15.0
Over 64 (Senescence—Senility)		(6.5 million)	6.8 (9 million)	9.0 (12 million)	14.4 (22 million)	17.0 (17 million)

viously no agreed purpose for man has as yet been formulated. He is muddling through. In spite of Mendel, he knows practically nothing about improving the race through heredity. A few of the unfit have been sterilized and some contraceptive clinics have been established, but the total benefit of eugenics to the human race so far is wholly negative, and euthanasia on any scale large enough to have an effect is as yet unacceptable to man's incipient humanity.

What gives these human values, which are still in the first stage of evolution, such a tremendous significance at this time is the current scientific revolution coming as it does immediately after the mechanical revolution. Mechanical and scientific technology permits these human values to go in the face of all the rules of biologic evolution. No species ever before has survived such outlawry against nature. The hope of Homo sapiens to survive lies in the unique position he holds by reason of his brain, which makes him the trustee of all life on earth but unfortunately also gives him the opportunity of sidestepping nature's laws. Furthermore no species ever has shown such remarkable adaptability to environment as this Homo, and this adaptability may in some way let him escape payment in the future for his present biologic errors.

Humanity, nevertheless, has preserved and nourished the moron, the feebleminded, the insane, and the criminal, and has allowed their intermarriage and reproduction until now the mass of human intelligence is being lowered instead of raised. The greatest of all biologic sinners, perhaps, is the physician, whose more recent scientific attainments give a power over life never intended by nature. He infringes the biologic rule of overproduction with survival of the fittest in the struggle for existence. Obstetrics and pediatrics have lowered infantile mortality to a minimum. The weak as well as the strong survive. Sanitation and artificial immunity are obligatory against extinction of the race. Medicine and surgery are fast eliminating one after the other the dangers of death from disease during adulthood, so that the day is near when every child born will expect to die of old age. There is no turning back. The only hope against what anthropologists decry as too much education is more education.

Every species has an optimum period of life. Someone has estimated this as six times the growth period. This rule would make the optimum period for man from 120 to 150 years of age, since bone growth is not finished before the twentieth to the twenty-fifth year. Medicine is now experimenting with a reticulo-endothelial serum which will prevent the present degenerations of old age and permit enjoyment of this optimum period of life to all normal individuals. At the present time, few men pass 100 even with the help of medicine, but with a cure for cancer, for hardening of the arteries, and for organic heart disease, all of which are reasonably possible, the medical profession will keep more and more people alive longer and longer. Imagine a nation such as the United States with a stationary population of 100 million people, the majority of whom reach 120 to 150 years of age—or even the assured 70?

One ray of hope not generally understood brightens this picture of gloom. Senescence does not necessarily mean a helpless decline and degeneration. The physical activity of an individual may reach the peak at around 40 years, but mental ability, the capacity for intellectual work from which are derived those human values which make men different from animals, is better at 60 than at 20 and declines only slowly afterwards (fig. 1). This fast growing surplus of intellectual power may be the evolutionary process which will save the race from early extinction, and when the physician with his biologic helpers solves the question of heredity, thus enabling the race to breed better brains as well as bodies, the odium now put upon the physician by anthropologists may in time be effaced. At present nothing is being done either to use effectively or to improve the intellect and

mature judgment of elders. Euthenics so far has been confined solely to improving the environment of youth. The recent increase in the number of old people creates the need for a well planned old age movement also.

Aging, after the physical peak is reached at around 40, progresses at different rates, rapidly in some individuals, slowly in others. A few people never realize they are growing old, but the majority definitely feel

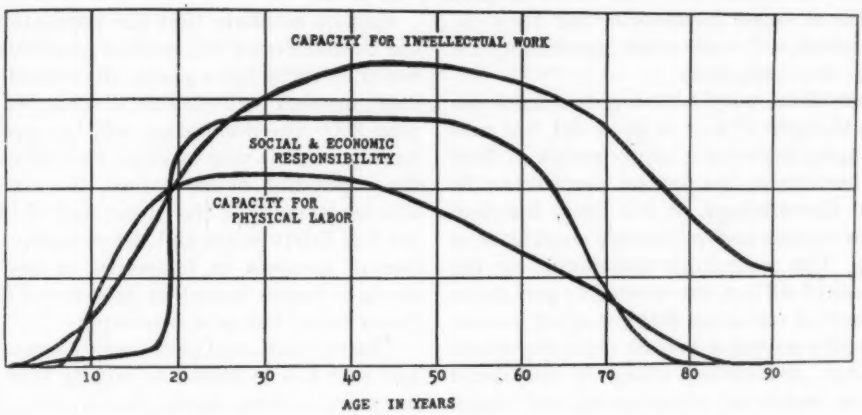

FIGURE 1.

This graph is reproduced from *Geriatric Medicine*, through the courtesy of the author, Dr. E. J. Stieglitz, and the publisher, the W. B. Saunders Company, Philadelphia.

age coming on. Usually a stage of senescence, a gradual decline, precedes that of true senility. There is no chronologic sequence, however, and some people at 50 are much older than others at 70. A set age for retirement, therefore, is often unfair both to the individual and to industry. The social status of elders at present is not satisfactory. On the farm, Grandpa would keep busy and useful, but not in the city, and there has been a tremendous shift from rural to urban life. The attitude towards old age has changed too. Age is not revered as formerly but is just more or less tolerated. In consequence almost everybody dreads the thought of growing old. The idea of the dependence of the aged is spreading, and society even contemplates giving everyone over 55 or 60 a pension for life. When medicine keeps people alive for another sixty or more years, what a mob of dependents there will be then. Social security of the pension kind is not at all the answer. The psychologic effect of frustration is no small factor in the overcrowding of asylums for the insane with the aged. The increase in the incidence of arteriosclerotic psychosis and senile psychosis is not altogether the result of the fact that many more people are now living to the age when these disorders are common. With a little encouragement, an individual can make the larger part of the later period of his life interesting to himself and useful to mankind. The stage of senescence can be prolonged by useful activity and true senility at the end made shorter and less frightening.

The problem of old age is both biologic and social. As an animal, man must eat and reproduce. As a human being, he must work and play. He toils for food and family first, but with these needs satisfied he then must be interested in or amused by something. No idle person ever was content. Throughout life man must be active or be bored. Activity can be manual or mental, but any social security with no outlet for muscle or brain is unbiologic. The significance of

leisure in old age is the opportunity of renewed activity, not the prospect of going from one rocking chair to another. Society must popularize this idea, furnish the opportunities for activity, and benefit by the results. There must have been plenty of leisure during the Golden Age of Pericles, but little if any idleness. Every individual of the future must begin at 40 to prepare himself for the inevitable period of senescence. Then when he has to let down or is forced to retire, he will have hobbies or other interests to fall back on, from which will come some opportunity for action and usefulness.

Heretofore, people have grown old without a thought of how to grow old, but now that aging deprives so many people of their past usefulness, the process needs scientific study. Gerontology, as this study is called, covers normal and pathologic conditions of aging. The pathologic conditions, or the diseases of old age, are covered by geriatrics, a branch of medicine. But the aging process of healthy people is a much more important problem, demanding study of the social aspects, industrial adjustments, and educational needs of normal older people. There has been practically no scientific research in gerontology. Now the time has come for an intensive study of the biologic processes of aging and the interrelation of these processes with changing social conditions.

Elders need to be classified as to abilities and disabilities. Many of the disabled may be moved into the active group through the aid of geriatrics, already a fast growing specialty. Tests to determine the particular aptitudes of the able elders can be developed. Social welfare clinics to advise and encourage the aged can be established. Opportunities for work, study, and play can be provided. Of first importance in a movement to make old age worthwhile is the development of schools or departments of gerontology which will institute the necessary research, will spread the philosophy that each individual should plan an active self reliance in old age, and will provide a scholastic program to meet the requirements. A school for elders is not too absurd. The majority are capable of being taught, and an active interest in a curriculum would not only make for happiness but would salvage ideas and intellect at a time when society needs them most. Instead of thinking "I'm through, I'm finished" upon retirement at 65 from whatever regular job a man has held, how much better were he to feel: "My life has just begun."

Summary

Experts estimate that the population of the United States will reach a maximum in less than forty more years, after which the total number will decline so that by the year 2000 the population will be approximately what it was in 1920. But whatever the population of the future, the remarkable lengthening of the expectancy of life in the last thirty years and the certainty of a further increase in longevity in the immediate future introduce into social life a factor never before encountered.

The proportion of persons 65 years of age and over has increased so rapidly that in a few more decades the elders will outnumber the youth of this country. So far the social sciences have done nothing for the aged. Politicians, probably because so few of them are biologically minded, have missed the significance of the problem. Social security, by which the aged will be classed as dependents, is not the answer. They cannot rightfully be pushed out as has-beens. Those intellectual values which are called human give older people the right to work and play usefully, not just for the purpose of killing time. Aging begins at 40 or thereabouts, and from then on each individual faces the problem of adjustment to the changing social conditions of his environment. Fortunately the capacity for intellectual work does not begin to diminish till near 60. At 60 it is better than it was at 30, better at 75 than at 20, and better at 90 than at 15. Because of the progress of medicine, an age of elders unknown to history has begun, and it is high time for society to recognize its significance and to

inaugurate an "old age movement" in self defence. Every healthy elder has some ability and should be given the opportunity to use it.

REFERENCES

1. Pearl, Raymond: *The Natural History of Population*. Oxford Univ. Press, New York, 1939.
2. Whelpton, P. K.: Population Policy for the United States. *J. Heredity*, 30: 401–406, 1939.
3. Stieglitz, E. J.: *Geriatric Medicine*. W. B. Saunders, Philadelphia, 1943.
4. Leake, Chauncey D.: Ethicogenesis. *Proc. Philos. Soc. Texas, Dec. 4, 1944*, Dallas, 1945.
5. Huxley, Julian: *Evolution—The Modern Synthesis*. Harpers, New York, 1942, p. 578.

Submitted for publication June 19, 1946

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The Effect of Aging on the Course and Outcome of Pregnancy

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OBSTETRICIANS HAVE TAKEN THE AGE OF 35 TO BE THE END OF YOUTH AND THE BEGINNING OF OLD AGE AS FAR AS HUMAN REPRODUCTION IS CONCERNED. THIS IS PARTICULARLY TRUE IN THE CASE OF THE PRIMIPAROUS WOMAN. DR. HELLMAN DISCUSSES THE EFFECT OF THE AGE OF THE MOTHER ON MATERNAL AND INFANT WELL-BEING IN BOTH PRIMIPAROUS AND MULTIPAROUS WOMEN AGED 35 TO 45 YEARS. THE HAZARDS TO PREGNANCY WHICH UNDOUBTEDLY INCREASE IN THIS AGE GROUP SHOULD SERVE AS WARNING POSTS THAT ADDITIONAL CARE MUST BE TAKEN WHEN THE MOTHER IS OVER 35.

THE matter of childbearing at either end of the normal reproductive period in a woman's life has attracted the attention and imagination of physician and layman alike. Down through the ages fabulous stories of children born to the very young and the very old recur with surprising regularity. The best known of these is the story of Sarah of the Old Testament, who, at 94 and long after the cessation of her menses, not only bore Abraham a son but was able to nurse this child. In Roman times, Cornelia of the family of Serpios is said by Pliny to have borne a son at 60. Gould and Pyle report numerous instances of fecundity in women of 50 and 60 years, a few at 70 and one at 103.

While it is impossible to say definitely that these reports are not true, it is worth noting that most of the instances of children being born to extremely old mothers occurred before the present century and at a time when the recording of births was unreliable. Certainly there was no constant means of checking the age of the mothers. In the experience of the Johns Hopkins Hospital, covering approximately 50,000 births, the greatest authenticated maternal age is 48. There is one record showing a mother with the stated age of 51, but a note appears in the history saying that the woman was feebleminded and that her statements could not be relied upon. It seems only reasonable that stories of pregnancy occurring much beyond the normal female reproductive period should be seriously questioned if not considered apocryphal.

Of much more practical importance, not only to the physician and to the mother but to the family unit and to the community, is the effect of the mother's age on the course and outcome of her pregnancy. This not only influences her efficiency as a member of the family but is also a limiting factor on how long and how well she will be able to care for her child. Beyond these rather intangible considerations, there is the effect of late occurring pregnancies on the life and health of both the mother and her infant. The following discussion is an effort to consider the influence of age alone on maternal and infant well-being, but it must be emphasized at the onset that both the parity of the mother and the spacing of her pregnancies are so intimately connected with the age factor that one cannot well be separated from the others.

Obstetricians have rather arbitrarily taken the age of 35 years as the end of youth and the beginning of old age as far as human reproduction is concerned. Particularly is this so in the case of the primigravida, who is termed elderly at 35. Much has been written concerning the peril both to her and to her child when pregnancy occurs at or beyond this age. Many seem-

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ingly radical procedures have been advocated to bring about a successful termination of her pregnancy. These procedures must be carefully evaluated not only in terms of maternal and infant mortality but also in the light of specific risks faced by mothers of this age group. These risks include, in addition to the medical complications of middle age, such as heart disease, kidney disease, and diabetes, the pregnancy complications of toxemia and myomata.

There is, furthermore, an additional hazard to the child. This hazard is, in reality, a twofold risk—that normally accruing to any first-born, plus the added danger of an aging mother. Thus, in figure 1, which shows the neonatal and stillbirth rate for over 45,000 deliveries where parity alone is considered, the rate is 57.7 per thousand viable deliveries for the first-born and is not again surpassed until the birth of the sixth child. The second part of the hazard to the infant of the elderly primigravida is demonstrated in table 1, which is taken from the scholarly paper of Yerushalmy (11). Here is presented not only an increasing infant death rate with advancing age of the mother, but the additional interposed factor of the in-

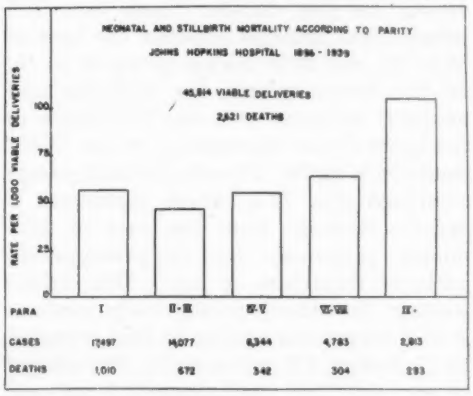

FIG. 1. Chart showing the relation of increasing parity to neonatal and stillbirth rates.

TABLE 1. (J. Yerushalmy, *Am. J. Hyg., 28:* 244, 1938.)

Frequencies of premature births and late fetal and neonatal mortality rates for 1,000 total births (including stillbirths) by age of mother for full-term and premature infants in New York State (exclusive of New York City), 1936.

Age of mother	Frequency of premature births*	Late fetal and neonatal mortality rates†		
		Total births	Full-term births	Premature births
Under 20	74.8	61.7	26.0	503.5
20–23	51.6	47.7	24.5	474.7
24–27	46.6	50.0	26.1	540.6
28–31	50.9	54.9	28.9	539.7
32–35	56.4	65.0	33.6	590.4
36–39	67.0	81.0	43.2	608.1
40 and over	85.5	112.7	62.4	650.0

* Per 1,000 total births (including stillbirths).
† Stillbirths and neonatal deaths per 1,000 total births (including stillbirths).

creased incidence of premature births and an increased vulnerability of these prematurely born infants correlated with the age of the mother. This latter factor exerts a very real effect on the statistics, for the death rate of premature children is between ten and twenty times that of term infants. The reason for this unexpected increase in the frequency of premature births and for the lack of vigor demonstrated by these infants is not apparent.

Another view of the problem may be taken from an analysis of 16,312 deliveries occurring at the Johns Hopkins Hospital during the last decade. There were 181 primiparous patients between the ages of 35 to 39, and 25 in the age group 40 to 45. In the former group, the stillbirth and neonatal mortality rate was 71.8, while in the latter it was increased to 80 per thousand viable births. The rate for both groups combined was 72.8, which represents a definite increase from the rate of 57.7 quoted previously for all primigravida patients regardless of age. This infant wastage for elderly primigravida mothers is of a magnitude similar to that reported by Galloway (7.8 per cent [5]), Wahrsinger (9 per cent [10]), Nathanson (3.2 per cent stillbirths [8]), and Daichman (4.1 per cent stillbirths [3]). All of these percentages are above the average for the clinics they represent, and are as low as they are only because of the special consideration given to the obstetrical handling of elderly patients.

In general, it has been the policy of the Johns Hopkins clinic and probably of the teaching clinics throughout the country to allow these older patients to deliver normally from below if the antenatal course, pelvis, presentation, birth canal, and labor are all normal. It has not been the experience here that the labors of older primiparous women are prolonged or more difficult than those of their younger sisters, nor is uterine inertia of a more frequent occurrence. However, the slightest deviation from normal, be it pelvic contraction, toxemia, malpresentation, myomata, or uterine inertia, deserves special consideration and frequently merits cesarean section. Thus in the age group 35 to 39 abdominal delivery was resorted to in 16 per cent of the cases, while in the 40 to 45 age group delivery was accomplished in this manner in 44 per cent of the cases. Inasmuch as the clinic average for cesarean section is 4 per cent, this incidence is admittedly high, and for the older group perhaps too high. It reflects not only an appreciation on the part of the obstetrician of the innate fetal risk involved, but also his awareness of the increased value of this opportunity given to a mother childless for two-thirds of her reproductive career. It is borne upon him too that this pregnancy is not only her first but perhaps her last chance at childbearing.

While the high incidence of section in the older group is not yet reflected, statistically, in an increased maternal mortality (there were 2 deaths in 206 deliveries), nevertheless this may be a fortuitous circumstance, and every effort should be made to reduce somewhat the incidence of this type of delivery. If cesarean section did guarantee 100 per cent infant survival, the high cesarean rate among older women might be permissible, but unfortunately this operation, even when done electively, carries with it a definite infant wastage rate. The aim of reducing the incidence of cesarean section is commendable, but must not be carried too far in delivering the elderly primigravida. Nixon reports 100 deliveries with but 1 cesarean section in primiparous women aged 40 to 45, with an infant and maternal death rate of 17 per cent and 4 per cent respectively. This whole problem requires a nicety of obstetrical judgment in order to balance evenly all the risks and still safeguard the patient's possible last chance of reproduction.

It would seem that the difficulties would be somewhat lessened in the case of the multipara in the older age group. Such is not the case, however, for though the pressure on the obstetrician to secure a good baby at all costs is somewhat reduced, the age factor is still present, and added to this

is the part played by parity, which has a natural tendency to increase with age. Figure 2 shows the increasing neonatal mortality rates with age where no attempt is made to consider parity. There is the usual high rate for the very young, with a low rate from the ages of 20 to 30, and then a gradual increase. Yerushalmy has attempted by statistical means, in an analysis of over seven million births, to separate the age from the parity factor (12). In figure 4 the dotted line shows the theoretical stillbirth ratio by age for multiparous women if the effect of parity is removed. The heavy line illustrates the percentage above or below the theoretical ratios where the actual observations fell. The dotted line still shows the typical U shape and rises slowly after the age of 25. The distance the heavy line lies above it after 30 represents the disadvantage attributable to parity. This parity effect is clearly demonstrated in figure 1, where the stillbirth and neonatal mortality rates of women with eight or more children are nearly two and a half times that of the low rates for second and third babies.

The fact that this rapid jump in infant mortality concomitant with parity is accompanied by a rise in the maternal mortality of three and a half times has led this clinic to offer women with eight full term pregnancies either contraceptive advice or puerperal sterilization. While this has seemed a radical innovation to some, it was done as a means of reducing the hazard to these multiparous women incidental not only to their large families but to their advancing age, which must of necessity accompany increasing parity. The basis of the maternal risk is again heart disease, kidney disease, and diabetes, while the immediate pregnancy complications are, as in the primiparous woman, toxemia and myomata. In the multiparous patient of high parity, several additional factors are

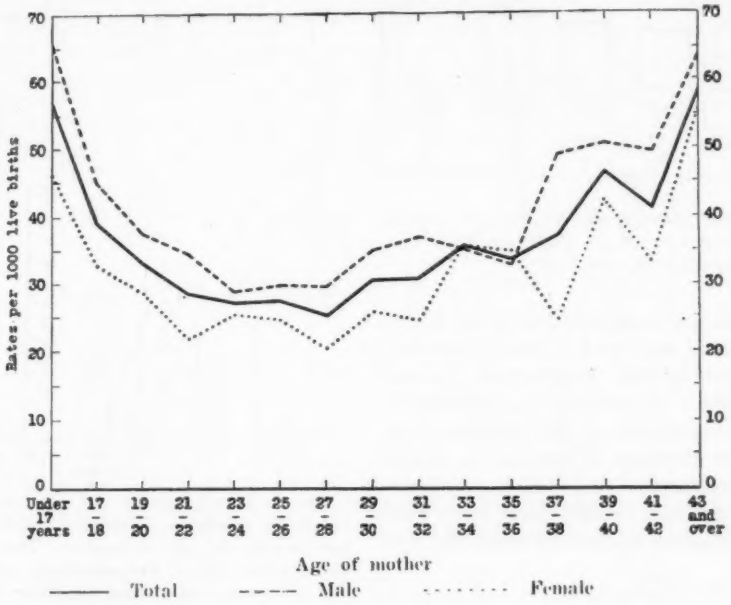

FIG. 2. Chart showing neonatal mortality rates per 1,000 live births by age of mother and sex of infant, New York State (exclusive of New York City), 1936. (J. Yerushalmy, *Am. J. Hyg., 28:* 244. 1938.)

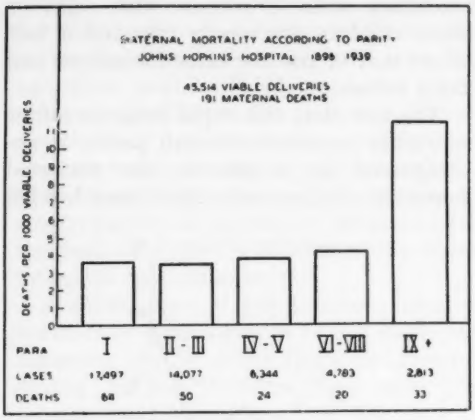
MATERNAL MORTALITY ACCORDING TO PARITY
JOHNS HOPKINS HOSPITAL 1895 1939
45,514 VIABLE DELIVERIES
191 MATERNAL DEATHS
DEATHS PER 1000 VIABLE DELIVERIES
PARA I II-III IV-V VI-VIII IX +
CASES 17,697 14,077 6,344 4,783 2,813
DEATHS 68 50 24 20 33

FIG. 3. Chart showing the relation of maternal mortality to parity. (N. J. Eastman, *New York State J. Med., 40:* 1708, 1940.)

added which are related to the relaxation of the abdominal wall and uterus. These are malpresentation and postpartum hemorrhage. There is, in addition, an increase in premature separation of the placenta, and spontaneous rupture of the uterus is also of higher incidence.

During the past decade there have been 1,025 multiparous women between the ages

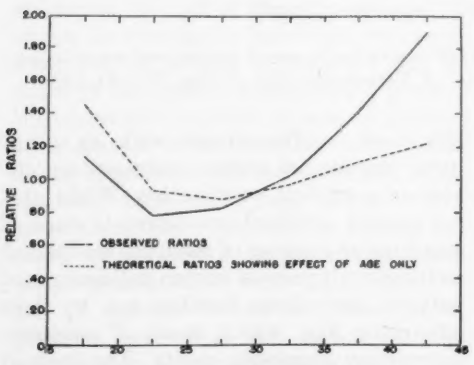

FIG. 4. Chart showing observed relative stillbirth ratios by age of mother and theoretical ratios when the effect of order of birth is eliminated, births to all multipara 15–44, United States, 1937–1941. (J. Yerushalmy, *Human Biology, 17:* 65, 1945.)

of 35 and 39 delivered of viable infants at the Johns Hopkins Hospital, with but 5 maternal deaths and a stillbirth and neonatal mortality rate of 74.1 per thousand viable births. In the age group 40 to 45, comprising 330 deliveries, the maternal mortality rate rose to 1.8 per cent and the combined fetal mortality rate to 123 per

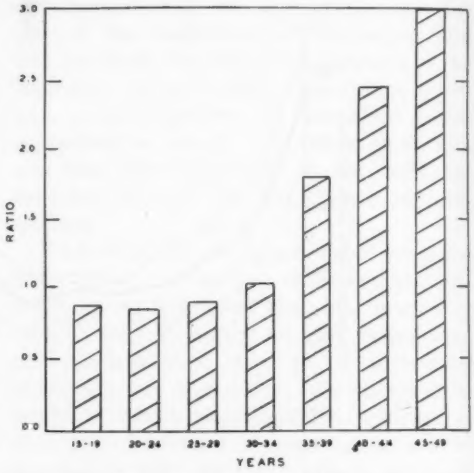

FIG. 5. Chart showing the relation of maternal age to the incidence of defective children. The base line records the age of mothers. The vertical line denotes the ratio of the percentage of defective to the percentage of normal children. (Douglas P. Murphy, *Am. J. Dis. Child. 51:*, 1007, 1936.)

thousand. If the two groups are taken together, the rates are 0.8 per cent and 8 per cent maternal and fetal deaths respectively. The increase in maternal deaths, as mentioned above, results not only from the increased incidence of heart disease, diabetes, and hypertension, but also from certain conditions peculiar to pregnancy in the 35 to 45 age-parity group. Figure 3 shows graphically a jump of three and a half times in the maternal death rate after the birth of the eighth child. Contributing to this increase in large degree is the incidence of hypertension and toxemia. When taken together these two conditions appeared in 22 per cent of the white, and 44 per cent of the colored, mothers aged 35 to

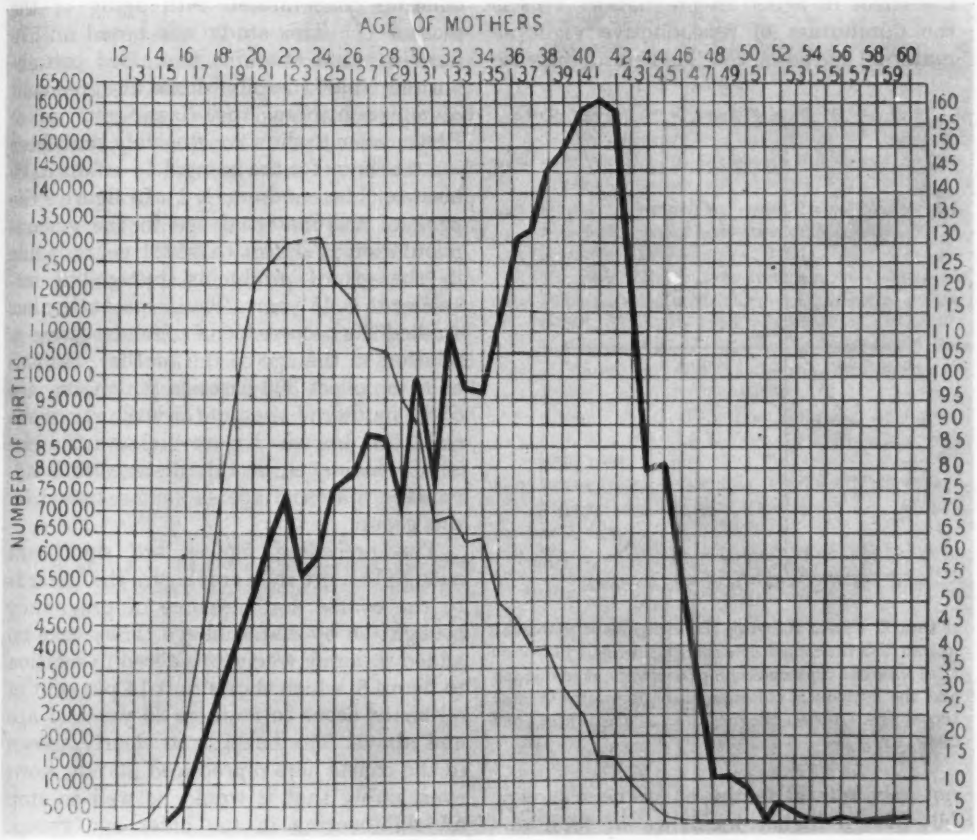

FIG. 6. Chart showing maternal age at birth of 2,822 mongoloid imbeciles compared with maternal age at birth of 2,000,000 children in the United States. (Adrien Bleyer, *Am. J. Dis. Child.*, *55*: 79, 1938.)

39, delivered here during the past decade. When the age group 40 to 45 is considered, hypertension and toxemia are increased to 35 per cent for the white and remain at 43 per cent for the colored mothers. This stationary rate for the colored mothers is in keeping with the impression that toxemia and chronic hypertension appear earlier and more frequently in this race than in the white.

The factors of malpresentation and premature separation are increased in the 35 to 45 age group and contribute not only to the maternal but also to the fetal death rate. These elderly mothers have shown an increase in abnormal presentations of all types, and the incidence of breech presentation in this group was nearly double the clinic average. Premature separation occurred in 1 per cent of the cases in the 35 to 39 age group and 2 per cent in the 40 to 45 age group, or twice as often as in multiparous women below the age of 35. There were seven instances of ruptured uterus in the 35 to 45 age group. This high rate is to be expected, as the uterine muscle tends to be replaced with fibrous tissue under the stress of both age and parity.

There is one additional factor which needs to be considered in a discussion of

the effect of aging on pregnancy. This is the diminution of reproductive vigor as maternal age advances. There is an increase

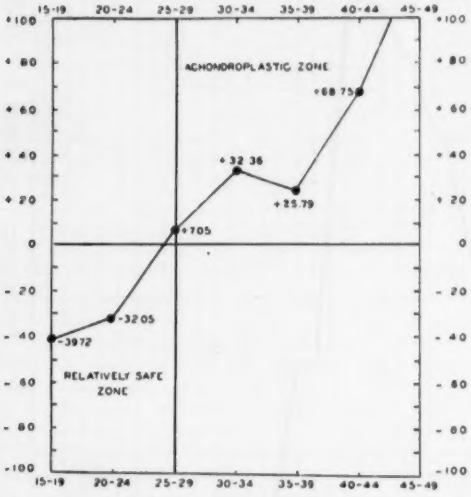

FIG. 7. Chart showing the relation of maternal age to the incidence of achondroplasia. The vertical columns represent the percentage of incidence and the horizontal columns quinquenniums of maternal age. (Adrien Bleyer, *Am. J. Dis. Child., 58:* 994, 1939.)

not only in fetal deaths, as has been shown, but also a higher incidence of fetal abnormalities and certain congenital diseases. The increased occurrence of these conditions begins shortly after 30 years, and children concomitant with aging of the mother (7). This study was based on 570 families, each of which contained one abnormal child. In spite of the disagreement of some authors, the classic studies of Bleyer seem to show conclusively that there is a tendency for the mongoloid infant to be born to older mothers (1, 2). In figure 6 the peak of the maternal age in the general population is shown to be 24 years, while in the group producing mongoloid imbeciles it is 41 years. The same author has studied the occurrence of achondroplasia in relation to the age of the mother. He was able to collect 303 cases in which the age of the mother at the time of the birth of the child was known. Figure 7 shows the rise in the incidence of this disease with advancing maternal age as demonstrated by this group.

The preceding figures are significant enough to more than emphasize the hazards to the course and outcome of pregnancy brought on by maternal age. They take on added meaning when considered in relation to figure 8, which shows that 14 per cent of all births occur to mothers 35 years of age and above. The hazards so clearly shown in the charts here reproduced do not, however, imply that it would be well to stop all childbearing in the older age group. They should serve as warning posts to the obstetrician and mother alike that there are dangers to be watched for, and that

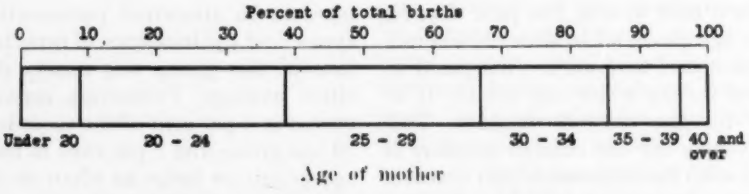

FIG. 8. Chart showing the percentage occurrence of births in relation to maternal age. (J. Yerushalmy, *Am. J. Hyg., 28:* 244, 1938.)

there can be no doubt that while parity may be of some significance, maternal aging is of prime importance. Thus, in figure 5 Douglas Murphy was able to show a definite increase in congenitally deformed additional care must be taken. They should serve also to show the young married woman that her greatest talisman in pregnancy is youth, and that the formation of her family should not be too long delayed.

Summary

The hazards of pregnancy, both to mother and child, increase with the age of the mother. Maternal and infant mortality rates increase, both in primiparous and multiparous women. The medical complications of middle age, such as heart and kidney disease, hypertension, and diabetes, and such complications of pregnancy as toxemia, myomata, and malpresentation, increase with the age of the mother and the number of children she has previously borne. In addition there is a higher incidence of fetal abnormalities and certain congenital diseases from the age of 30 onwards. Since 14 per cent of all births occur to mothers 35 years of age and above, these hazards of pregnancy are most important and should be carefully watched.

References

1. Bleyer, A.: The Role of Advancing Maternal Age in Causing Achondroplasia. *Am. J. Dis. Child., 58:* 994–1000, 1939.
2. Bleyer, A.: The Role of Advanced Maternal Age in Causing Mongolism. *Am. J. Dis. Child., 55:* 79–92, 1938.
3. Daichman, I.: Labor in Elderly Primigravida. *Am. J. Obst. & Gynec., 24:* 127–132, 1932.
4. Eastman, N. J.: Hazards of Pregnancy and Labor. *New York State J. Med. 40:* 1708–1712, 1940.
5. Galloway, C. E., and Paul, T. D.: A Study of 288 Primiparas Over the Age of 35 Compared with 300 Primiparas Under the Age of 25. *Am. J. Obst. & Gynec., 36:* 255–259, 1938.
6. Gould, George M., and Pyle, Walter L.: Anomalies and Curiosities of Medicine. W. B. Saunders, Philadelphia, 1897.
7. Murphy, D. P.: Maternal Age at Conception of Congenitally Malformed Child. *Am. J. Dis. Child., 51:* 1007–1013, 1936.
8. Nathanson J. N.: A Parallel Study of Labor in Young and Old Primiparas. *Am. J. Obst. & Gynec., 30:* 159–173, 1935.
9. Nixon, W. C. W.: The Influence of Age on Labor. *J. Obst. & Gynaec. Brit. Emp., 38:* 821–826, 1931.
10. Wahrsinger, P. B., and Kushner, J. I.: Elderly Primigravida. *Am. J. Obst. & Gynec., 44:* 505–509, 1942.
11. Yerushalmy, J.: Neonatal Mortality by Order of Birth and Age of Parents. *Am. J. Hyg., 28:* 244–270, 1938.
12. Yerushalmy, J.: Interval Between Successive Births and Its Effect on Survival of Infant. *Human Biol., 17:* 65–106, 1945.

Submitted for publication August 8, 1946

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The Effect of Coffee, Human Diets, and Inheritance upon the Life Span of Rats

GLADYS A. SPERLING, J. K. LOOSLI, L. L. BARNES, AND CLIVE M. McCAY

TO DETERMINE THE EFFECT OF DIET AND OF COFFEE UPON THE LIFE SPAN OF WHITE RATS, THE LABORATORY ANIMAL MOST SIMILAR TO MAN IN NUTRITIONAL HABITS, MISS SPERLING, DR. LOOSLI, DR. BARNES, AND DR. MCCAY FOLLOWED THE LIFE SPAN OF GROUPS OF RATS FED UPON (1) A DIET EQUIVALENT TO THAT CONSUMED BY MANY PEOPLE, (2) THAT SAME DIET "IMPROVED" BY THE ADDITION OF WHOLE WHEAT BREAD AND CERTAIN MEATS AND VEGETABLES, AND (3) THE FIRST DIET SUPPLEMENTED WITH VITAMINS. COFFEE WAS GIVEN TO HALF OF EACH DIETARY GROUP, WATER TO THE OTHER HALF. NEITHER DIET NOR COFFEE HAD MUCH EFFECT ON THE LIFE SPAN, BUT THE HEREDITY OF THE RATS HAD A DEFINITE EFFECT.

CHANGES in the diet of the people of the United States are taking place constantly. The student of nutrition develops a part of his philosophy in this respect from experience with animals. A few of these changes are based upon obvious human needs, such as the need for vitamin supplements to prevent a specific disease like pellagra. Many more changes in diet are made because experiments with animals during some period of life—for instance, the growth period—have indicated a favorable response to some dietary supplement throughout this period. Other changes are recommended because experiments with a few human beings for brief periods have indicated the influence of certain factors. These influences may be expressed in various ways, such as by a poorer absorption of calcium in the course of a balance study.

A major influence in changing food habits is advertising. In this case, the change in diet is the result of some special group's desire for profit by selling a given foodstuff or beverage.

Within recent years a widespread attempt has been made to improve human nutrition by increasing the level of some of the water-soluble vitamins and iron in bread and other cereal products. During this period fewer cases of deficiency diseases have been observed by some clinicians in areas such as New York City. Some observers have attributed this to the enriched bread. Neglected, however, have been the increased purchasing power and the more general use of meats, eggs, and milk during this same period of years.

Few attempts have been made to test the recommendations of nutritionists for the improvement of human dietaries, by feeding mixtures of foods in the proportions consumed by man, to animals throughout the whole life span. However, in one series of experiments with white rats an attempt was made by us (1, 2) to compare the effects of supplementing a basal diet of moderate quality with four common human foodstuffs—namely, starch, sucrose, meat and milk. No evidence was found that these supplements extended the span of life. The source of calories seemed to be a matter of little importance if an adequate basal diet were consumed.

In contrast, the experiments of Sherman and Campbell (5) indicated that a "higher

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Dr. LeRoy L. Barnes is associate professor of biophysics at Cornell University. He received his A.B. degree at Oberlin in 1926 and his Ph.D. from Cornell in 1932.

Dr. Clive M. McCay has been professor of nutrition at Cornell University since 1934. He received his A.B. degree from the University of Illinois in 1920, his M.S. from Iowa State College in 1923, and his Ph.D from the University of California in 1925. He has taught at the University of Texas, Iowa State College, the University of California, and Yale.

The studies reported on in this paper were carried out with the aid of grants by the Federal Government, the State of New York, and the Rockefeller Foundation. Expert technical assistance was rendered by Mrs. Vonda McCloskey, Mrs. Ruth Seither, and Mr. Alfred Armitage.

The sources of the vitamin supplements used were "Napco XX" and "Vitab," made by the National Oils Products Co., Harrison, N. J.

degree of health" and an "increased length of life" resulted from supplementing a basal diet of wheat and milk with additional sources of calcium, vitamin A and "vitamin G." However in neither our experiments nor those of Sherman and Campbell did the basal diets resemble closely those consumed by man.

In all such studies with white rats, the inherent weakness in drawing conclusions for human application is that one dominant chronic disease largely determines the span of life of the white rat. This disease is bronchiectasis (4). In the last analysis, when white rats are employed to determine the effect of diet upon the span of life, the real study may be the effect of diet upon bronchiectasis, although several other degenerative diseases add to the complications of such research.

In spite of the differences between the chronic diseases that beset man and the white rat during the latter half of life, the rat is the most useful animal known today for research purposes. Its nutrition has been studied extensively and compares closely with that of man. Its normal life span is about two years, so that a number of generations can be studied during the working life of a man. Some of the pathologic conditions that develop in the rat during the latter half of life compare with those found in man (4).

Material and Methods

The purpose of the present study was to determine the effect upon longevity in the rat, of "improving" the diet commonly consumed in the northeastern part of the United States. A basal diet "A" was designed from human foods proportioned according to those known to be consumed (7, table 1). A second diet "B" was "improved" by including twice as much whole milk, meat richer in vitamins, such as liver, more carrots, and less sugar and potatoes. In lieu of additional green, leafy vegetables, which were difficult to secure regularly during the winter in wartime, a substitution was made in diet B by the addition of 1 per cent of alfalfa leaf meal. This is the only item not commonly used in human food.

A third diet consisted of the basal mixture A, supplemented with the following vitamins, per rat weekly: A—840 I.U.; B_1—300 μg; riboflavin—20 μg; pyridoxin—300 μg; pantothenic acid—550 μg; nicotinic acid—4 mg.; filtrate factor—54 units.

In order to make this experiment accord further with human practices, each diet was fed to groups with and without a modest supplement of coffee brewed fresh each

day. This coffee was prepared in the usual manner by brief boiling, allowing one tablespoon of coffee per cup. Rats were not given the coffee until well grown at six months of age. Each rat ingested 3 ml. daily.

TABLE 1. DIETS SIMILAR TO THOSE EATEN BY PEOPLE IN THE UNITED STATES

Components	A	B
	(lbs.)	(lbs.)
Eggs, cooked	3.0	3.0
Whole dry milk	4.0	8.0
Fat (oleomargarine)	2.0	2.0
Butter	2.0	2.0
Hamburg, cooked	10.0	5.0
Liver, cooked	—	5.0
Pork sausage, cooked	4.0	4.0
Sugar	6.0	4.0
White bread, unenriched	16.0	—
Whole wheat bread	—	16.0
Potatoes (Irish), cooked	31.7	23.7
Tomatoes (canned)	3.0	5.0
Carrots (fresh)	7.0	10.0
Beans (navy), boiled	1.0	1.0
Apples (fresh)	10.0	10.0
Sodium chloride	0.3	0.3
Alfalfa leaf meal	—	1.0

For this study 240 weanling rats were divided into six groups, with distribution based upon litter mates and sex. Throughout the experiment they were housed in air-conditioned rooms at 23 C. Natural light was excluded. Artificial light was turned on automatically each morning at six and off twelve hours later. Because of a fire in an adjoining building the rats were moved from one building to another when about 320 days of age. A few were lost during this transfer as is indicated in table 2.

During the first six months of this study the growth of the bones was measured by x-ray photographs.

RESULTS

Growth curves of body weight data and x-ray photographs of the tibia both indicate a more rapid growth rate for rats receiving the supplemented diets, B and C (fig. 1).

Individual life span data are presented

TABLE 2. EFFECT OF COFFEE UPON LIFE SPAN OF RATS
(Age at death is expressed in days; + =with coffee, − =without)

Females						Males					
A+	A−	B+	B−	C+	C−	A+	A−	B+	B−	C+	C−
303	304	272	315	343	327*	75	93	297*	317	301*	311
382	327*	398	413	525	376	198	282	323*	325*	323*	324*
467	332*	414	435	536	378	261	328*	347	350	326*	348
636	339	419	512	640	383	326*	329*	417	408	335	354
663	347	434	541	688	470	343	330*	474	495	392	363
671	466	501	569	716	474	457	488	497	536	431	417
757	469	523	600	732	*474	457	494	511	620	435	443
762	489	575	617	741	522	525	505	554	620	507	528
802	501	603	669	748	577	561	558	573	633	521	546
826	517	638	679	795	665	589	602	593	641	568	583
850	530	656	712	799	690	602	620	599	660	655	603
853	595	712	738	813	691	622	643	606	667	666	645
856	672	720	747	853	727	667	670	609	676	726	662
900	753	720	776	904	737	690	671	658	689	729	665
905	806	726	778	929	753	694	688	676	695	741	706
974	816	730	784	959	755	707	691	678	761	764	796
978	821	750	799	967	799	711	778	689	783	778	799
1018	823	802	806	1069	828	715	831	711	857	801	812
1057	833	956	810	1122	866	737	890	726	911	878	819
1062	903	1033	889	1263	1024	900	950	801	927	951	1007

* Lost due to removal to another laboratory during a fire in an adjoining building.

(table 2) since few data of this type are available for critical study.

The summarized data for the life span (table 3) afford no evidence that there were significant differences among groups fed diets A, B, and C. Although life span is only one criterion of an optimum diet, it affords evidence that diets were not improved by the addition of more vitamins and calcium. Furthermore, there is no evidence that the slower growth rate of group A modified the result although this slower growth rate might have been the factor that masked any improvements introduced into diets B and C. Thus the life span of group A may have been improved by the slower growth rate to the same extent that diets B and C extended the span due to better quality of the diets. This all seems unlikely in the light of past results, however, inasmuch as all data for life span fall within the same zone of values established by us and others, while the mean or extreme values for the span of life do not approach those found earlier for rats severely retarded in growth.

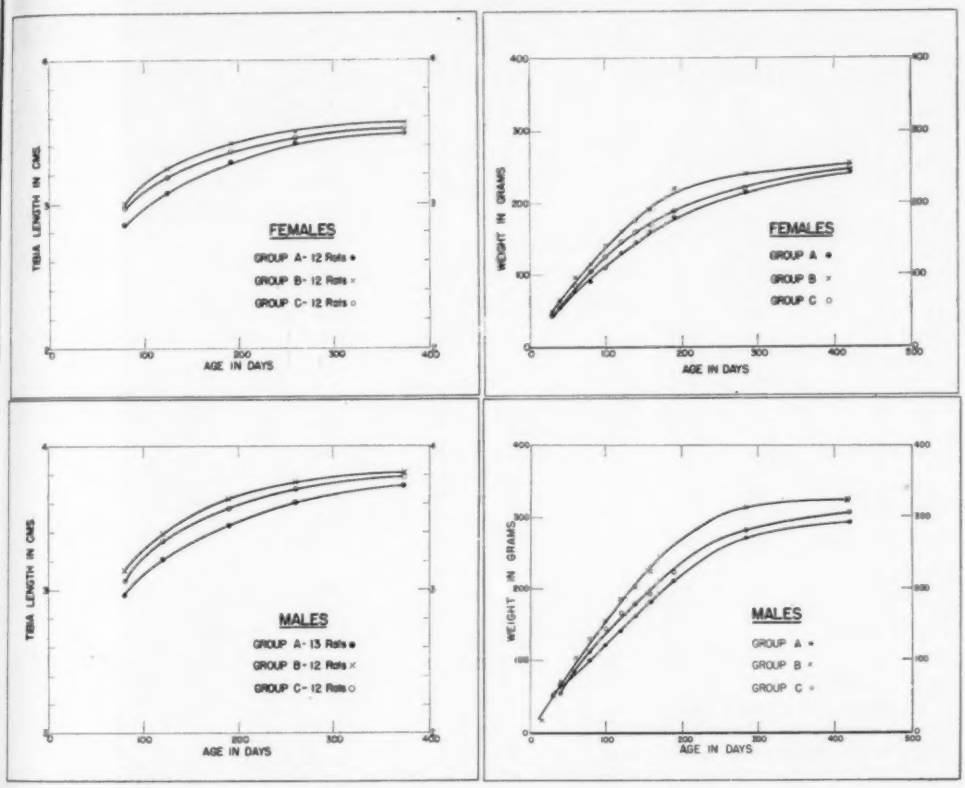

FIG. 1. Rate of growth of rats fed a diet of human foods (A), this diet "improved" with natural foods (B), and the diet supplemented with vitamin concentrates (C).

It does not seem justifiable to draw conclusions from data of this type or the data presented by Sherman and Campbell (6) concerning the rate of growth and the total life span, for comparison with studies of retarded rats fed diets deficient only in

calories. In our present experiments growth rates were probably influenced by borderline deficiencies that did not come into the picture of growth for rats restricted only in calories. Likewise, data attempting to correlate the span of life with rate of growth life span for any group. In fact, two of the three groups of females seemed to respond favorably to the supplement of coffee (table 3). Differences are significant according to conventional methods of testing, although we have come to have doubts

TABLE 3. EFFECT OF DIET AND COFFEE UPON LIFE SPAN OF RATS

Group	Diet*	Coffee	No.	Sex	Mean life span, days	PEM†	D/PE‡
1	A	−	20	F	582	30	
2	A	+	20	F	786	31	
1 and 2			40	F	684	43.1	5
3	A	−	20	M	572	32	
4	A	+	20	M	542	31	
3 and 4			40	M	557	44.5	<1
5	B	−	20	F	659	23	
6	B	+	20	F	629	28.5	
5 and 6			40	F	644		<1
7	B	−	20	M	629	26.6	
8	B	+	20	M	567	20.6	
7 and 8			40	M	598		1.8
9	C	−	20	F	626	28.6	
10	C	+	20	F	807	32	
9 and 10			40	F	716		4+
11	C	−	20	M	587	29.8	
12	C	+	20	M	591	30.2	
11 and 12			40	M	589	42	<1

* A—Average diet.
B—Improved average diet.
C—Average diet plus vitamins.
† PEM—Probable error of the mean.
‡ D/PE—Difference divided by the probable error.

when rats are raised upon the same diet under similar conditions are not comparable to data obtained from rats raised upon diets restricted in calories, because in the former case sickly rats tend to grow slower and die younger. In the case of comparisons between animals with a normal growth rate and those with a low calorie, retarded growth rate, this variable is balanced between groups by the selection of experimental animals at the beginning.

Furthermore, a summary of our data gives no evidence that coffee shortened the concerning the application of the usua statistical treatment to data of this type unless experiments are repeated.

Effect of Coffee upon Breeding, Lactation and Growth of Young.—Inasmuch as many claims have been made that coffee has deleterious effects upon men and animals (8), and since our preceding experiments afforded no such evidence, additional exploratory studies were started while the first work was still in progress.

Preliminary data were sought upon the effect of moderate amounts of coffee upon

growth, reproduction, and lactation. Three groups of adult female rats about 4 months of age were fed the stock diet used in our colony (G.L F. Calf Meal). As the sole source of liquid, one group was given strong coffee (one tablespoon coffee per cup of water); one, weak; and one, water. The "weak" was half as strong as the other mothers fed strong coffee was slightly less, but differences disappeared as the rats matured. These rats in turn were used to produce a third generation. No differences resulted. No evidence was found that coffee modified growth or reproduction.

Inheritance as a Factor in Studies of Aging.—The importance of inheritance as a factor in human longevity has long been recognized. In our nutrition studies, attempts have been made to equalize this factor by the assignment of individuals from the same litter to different groups. In the first section of the present study, careful note was made of the relation between the life span of individuals (table 2) and the litter of origin. A record had been kept of the dam but not the sire for each litter.

TABLE 4. EFFECT OF INHERITANCE FACTOR ON LONGEVITY OF THE RAT

Group	Number of litters	Total weaned	Used in experiments	Distribution of deaths (days)			
				Under 500	500–700	Over 700	Lost
I. Providing 4 or more rats	33	191	173	33	59	75	6
(a) Short lived (Under 500 days)	4	23	20	14	4	1	1
(b) Long lived (Over 700 days)	11	64	59	8	6	44	1
(c) Average (500–700 days)	18	104	94	11	49	30	4
II. Providing less than 4 rats	28	93	67	18	22	18	9
Total (I and II)	61	284	240	51	81	93	15

coffee. The average daily consumption per rat for the three fluids was: strong coffee, 29 ml., weak coffee, 32, and water, 26. Unlike sucrose beverages, coffee does not seem especially attractive to rats, and the amount consumed is approximately the same as water (3).

After five weeks of this regime, males were placed in the cages. Eleven litters were produced in each group from this mating. Breeding of the females was continued at intervals of three months. All but one female (on water) produced at least one litter during the first year. In old age these females were used for other studies, but there was no evidence that coffee shortened the span of life.

A second generation of rats from these mothers was raised upon a similar diet and beverages. The growth of the young from

A summary of these data (table 4) indicates that 6.5 per cent of the litters accounted for 27 per cent of the short-lived rats that died within 500 days. In contrast, 18 per cent of the litters provided for 47 per cent of the long-lived animals that died after 700 days of age.

Inheritance seems to play an important role in determining the life span of the rat. Whether or not this factor acts through an

increased resistance to the chronic diseases of the rat, such as bronchiectasis, cannot be determined from this study.

Summary

Three diets were fed to groups of eighty rats throughout life. One diet resembled that eaten by many persons in northeastern United States. A second diet was similar to this but supposedly better because of the inclusion of more whole wheat bread, milk, and liver. A third was supplemented with vitamins. Each diet was fed with and without a moderate supplement of coffee, equal to about a cup per person per day. Life span data afforded no evidence for the superiority of any of the three diets. Coffee at this low level was not injurious and may have had a favorable effect upon the survival of the females. An auxiliary study in which coffee was fed as the sole source of fluid during lactation and the growth of three generations, afforded additional evidence that even large amounts exerted no unfavorable effect. Evidence is presented that inheritance exerts a definite influence upon the length of life of the white rat.

References

1. McCay, C. M., Sperling, Gladys, and Barnes, L. L.: Growth, Ageing, Chronic Diseases, and Life Span in Rats. *Arch. Biochem., 2:* 469–479, 1943.
2. McCay, C. M.: Nutrition, Ageing and Longevity. *Tr. & Studies College of Physicians, 10:* 1–10, 1942.
3. Restarski, J. S., Gortner, R. A., and McCay, C. M.: Effect of Acid Beverages Containing Fluorides upon the Teeth of Rats and Puppies. *J. Am. Dent. A. 32:* 668–675, 1945.
4. Saxton, J. A., Jr.: Nutrition and Growth and Their Influence on Longevity in Rats. *Biol. Symposia, 11:* 177–196, 1945.
5. Sherman, H. C., and Campbell, H. L.: Further Experiments on the Influence of Food upon Longevity. *J. Nutrition, 2:* 415–417, 1930.
6. Sherman, H. C., and Campbell, H. L.: Rate of Growth and Length of Life. *Proc. Nat. Acad. Sc., 21:* 235–239, 1935.
7. Stiebling, Hazel K., and Coons, C. M.: Present Day Diets in the United States. *Yearbook of Agriculture,* 296–320, 1939.
8. Teply, L. S., Kiehl, W. A., and Elvehjem, C. A.: Studies on the Nicotinic Acid Content of Coffee. *Arch. Biochem., 6:* 139–149, 1945.

Submitted for publication July 20, 1946

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The Size of Somatic Chromosomes at Different Ages in the Rat

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DR. BIESELE HAS PUBLISHED A NUMBER OF PAPERS ON CHROMOSOMAL CHANGES—IN RELATION TO B VITAMINS, RIBONUCLEIC ACID, AND NUCLEAR VOLUME; IN EPIDERMAL CARCINOGENESIS; AND NOW IN THE SIZE OF CHROMOSOMES AT DIFFERENT AGES IN THE RAT. VARIABILITY IN CHROMOSOME SIZE WAS OBSERVED FROM METAPHASE TO METAPHASE, IN DIFFERENT TISSUES IN THE SAME ANIMAL, IN THE SAME TISSUE IN DIFFERENT ANIMALS OF THE SAME AGE GROUP, AND IN THE SAME TISSUE IN ANIMALS OF DIFFERENT AGE GROUPS. THE LEAST VARIABILITY WAS OBSERVED IN EMBRYONIC ANIMALS, THE GREATEST IN THE OLD ANIMALS.

THIS survey was undertaken in order to learn how the size of somatic chromosomes in a mammal varies at different ages in different cell types, and may be regarded as a morphologic approach to the problem of the function of chromosomes in the economy of the cell from embryonic life to old age. The study also provides a more adequate background for the observation of chromosomal enlargement in cancerous tissues (8, 9, 5, 4).

MATERIAL AND METHODS

Material was obtained from 44 albino rats of the Wistar colony. There were from 4 to 7 animals in each of the following age groups: late embryonic, newborn, 12 day old, 3 week old, and 3 month old (84 and 94 days); and there were 17 "3 year old" animals from 844 to 1058 days of age. The data from the 84 day old male, published earlier (3), are included here.

Specimens from the killed animals were fixed at autopsy by the group of skilled dissectors in the Wistar Institute. After the specimens had been in a 3:1 alcohol-acetic acid solution for a period of from several hours to several days and had been stored for irregular intervals in 83 per cent alcohol, acetocarmine squash preparations were made, dehydrated in alcohol, and mounted in diaphane.

The microscopic study was carried out with oil immersion and green light. Measurements were made to the nearest quarter-micron. This was close to the limit of resolution of the optical system.

For each mitotic figure at or close to metaphase that was analyzed, an average volume of the chromosomes was calculated. By means of a millimeter ruler on the drawing surface beneath the camera lucida mirror, the maximum width of chromosome in the figure was measured (i.e., across both chromatids of the bicylindrical metaphase chromosome). One-fourth of this measurement was recorded as the chromatid radius and entered, together with the average chromosome length measured on the outline drawing, into a formula for the volume of a pair of twin cylinders. The value arrived at, calculated to the nearest tenth cubic micron, was called the average chromosome volume (5).

The number of metaphases thus analyzed was ten in most specimens, though it was less in some of the older animals and more in others. Significance of difference between means was determined by means of the "t" test.

Chief attention was paid to the liver (hepatic epithelium), kidney (tubules of the cortex), epidermis, lung (nonepithelial cells), small intestine epithelium, and mesenteric lymph node. Specimens of spleen, thymus, and adrenal were also studied in certain age groups exclusive of the old animals. Since the preparation involved a pressing out, the exact localization of the mitotic figures was lost. Al-

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This work is part of a general study on aging organized by Dr. E. J. Farris of the Wistar Institute of Anatomy and Biology, with the aid of cooperating scientists and with the support of the Samuel S. Fels Fund. The author began the study at the Department of Zoology of the University of Pennsylvania.

though epithelial elements tended to cohere and cell shape and relative quantity of cytoplasm could be distinguished at times, considerable uncertainty in identification of cell types must be recognized.

The possibility of error was present also in the measurements, since the work was done near the limit of resolution; in the perhaps-variable swelling or shrinking of chromosomes fixed or stored over different periods of time; in the degree of pressing out of the mitotic figures in making the squash preparations; and also in the selection of figures in the correct mitotic stage. Obviously, the "average chromosome volume" was reached by means of several approximations, and it would probably have been different with other fixatives or in life.

Observations

Within each specimen, variability in chromosome size was observed from metaphase to metaphase. Some of the variability was attributable to difference in cell type, but mitotic figures of the same cell type also differed. The maximum average chromosome volume observed in a given specimen was usually twice as large as the minimum and sometimes five or six times as large.

Within the same animal, there were often significant differences between the means of the average chromosome volumes from one organ or tissue to another. This confirmed an earlier and less extensive study made in 1944 (3).

Within an age group, variations in chromosome size in a given tissue occurred from one animal to another. That this source of variation was not of great moment, however, was indicated by an analysis of variance for the 240 metaphases drawn from kidney, liver, lung, lymph node, small intestine, and spleen of the four animals 12 days old; the variation from organ to organ was about twelve times as important as the variation between rats in making up the total variation in chromosome size.

The fourth source of variability, age, commands attention. Figure 1 shows the average chromosome volumes for six organs studied in the six age groups. It will be observed that the overall variability was least

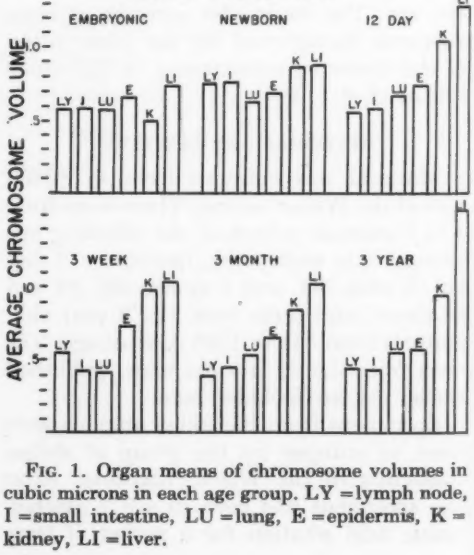


Fig. 1. Organ means of chromosome volumes in cubic microns in each age group. LY = lymph node, I = small intestine, LU = lung, E = epidermis, K = kidney, LI = liver.

in the embryonic or newborn animals and most extensive in the 3 year olds. The change was occasioned by enlargement of chromosomes in some organs and diminution in others.

Each tissue followed its more or less individual pattern of changes in chromosome size with age. Roughly, there were three sets of patterns.

First were those patterns exhibiting considerable uniformity throughout life. The epidermis, for example, maintained chromosome volume means of about 0.7 cubic micron through all stages until the pos-

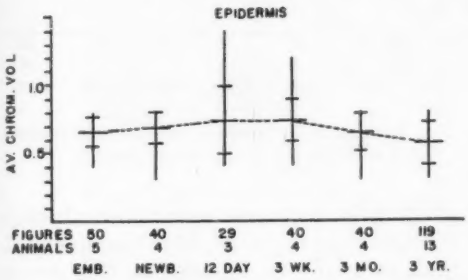


FIG. 2. Variation of average chromosome volume with age in epidermis. The vertical bars represent range of average volumes per metaphase in each group, the longer horizontal bars connected by dash lines represent the group means, and the shorter horizontal bars mark off one standard deviation on each side of the mean.

sibly significant decrease in old age (figs. 2, 10). The nonepithelial cells of the lung had chromosomes significantly reduced in size below the other stages at 21 days only (figs. 3, 11, 12).

The second set of patterns involved an increase in size of chromosomes near birth and a decrease in later stages. The epithelium of the small intestine had a statistically significant rise in size of chromosomes at birth and successive significant drops at 12 and 21 days to a mature level below the embryonic level (figs. 4, 13, 14). There was much pyknosis in the small intestines of the older animals, and in most of them, epithelial mitoses were not evident. The lymphoid tissues also had this

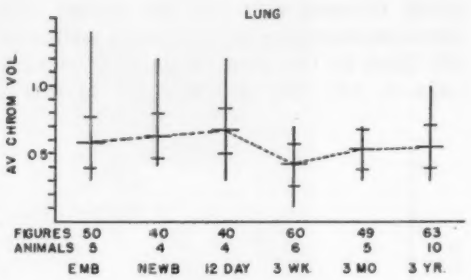


FIG. 3. Variation of average chromosome volume with age in nonepithelial cells of the lung.

type of pattern. In the mesenteric lymph node, chromosomes were larger at birth, were down to the embryonic level at 12

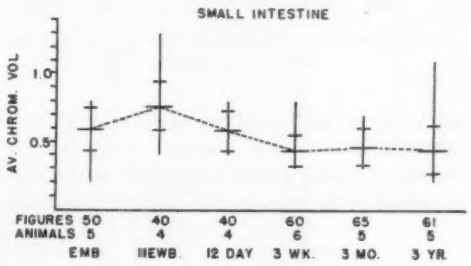


FIG. 4. Variation of average chromosome volume with age in small intestine epithelium.

and 21 days, and had undergone a further significant drop by the 3 months' period (figs. 5, 15). Mitotic lymphocytes in the small intestine of senile rats had very

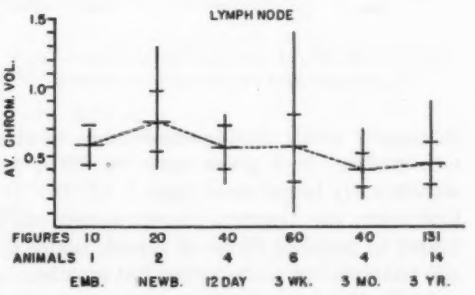


FIG. 5. Variation of average chromosome volume with age in mesenteric lymph node.

small chromosomes. In the spleen the chromosomes were larger in early postnatal life than in the embryo or at 3 months (figs. 6, 16). Big chromosomes in mega-

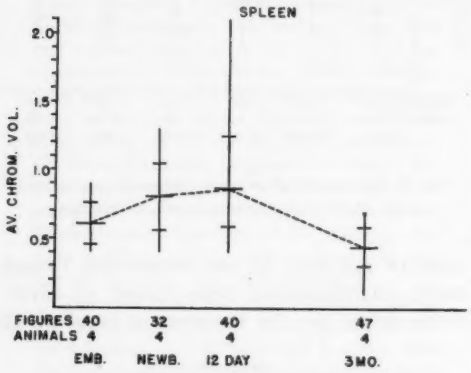


FIG. 6. Variation of average chromosome volume with age in spleen.

karyocytes and in other cell types as well contributed to the greater range in the spleen of young animals. In the rat thymus, of which only two stages were studied, the

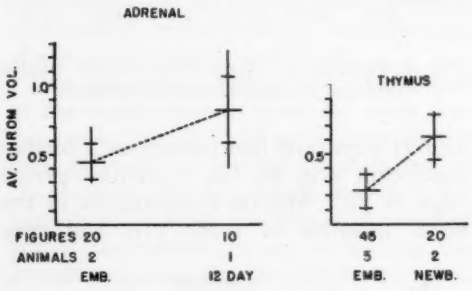


FIG. 7. Variation of average chromosome volume at younger ages in adrenal and thymus.

extremely small chromosomes seen in the late embryo had given way by birth to significantly larger ones (figs. 7, 17, 18). In C58 mice the thymus chromosomes were found to parallel those of lymph nodes in age changes but to be somewhat smaller.

In the third set of patterns, chromosomes increased in volume after embryonic life to a maintained or increased high level. The adrenal probably belonged here, according to scanty evidence in Wistar rats (fig. 7) and observations in an adult male Osborne-Mendel rat (3). The kidney had this type of pattern, with progressive enlargements of chromosomes at birth and

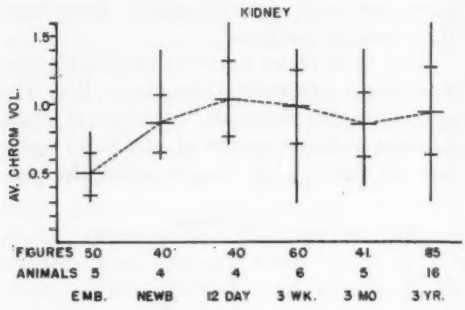


FIG. 8. Variation of average chromosome volume with age in kidney cortex tubules.

at 12 days to a size maintained through old age (figs. 8, 19, 20, 21). The liver epithelium might be included in this group, despite its high variability (figs. 9, 22, 23, 24). Beginning in late embryonic life with the largest chromosomes, the liver retained its relative position at all ages. In

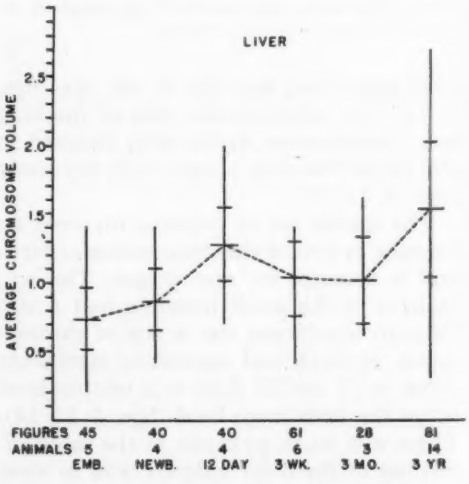
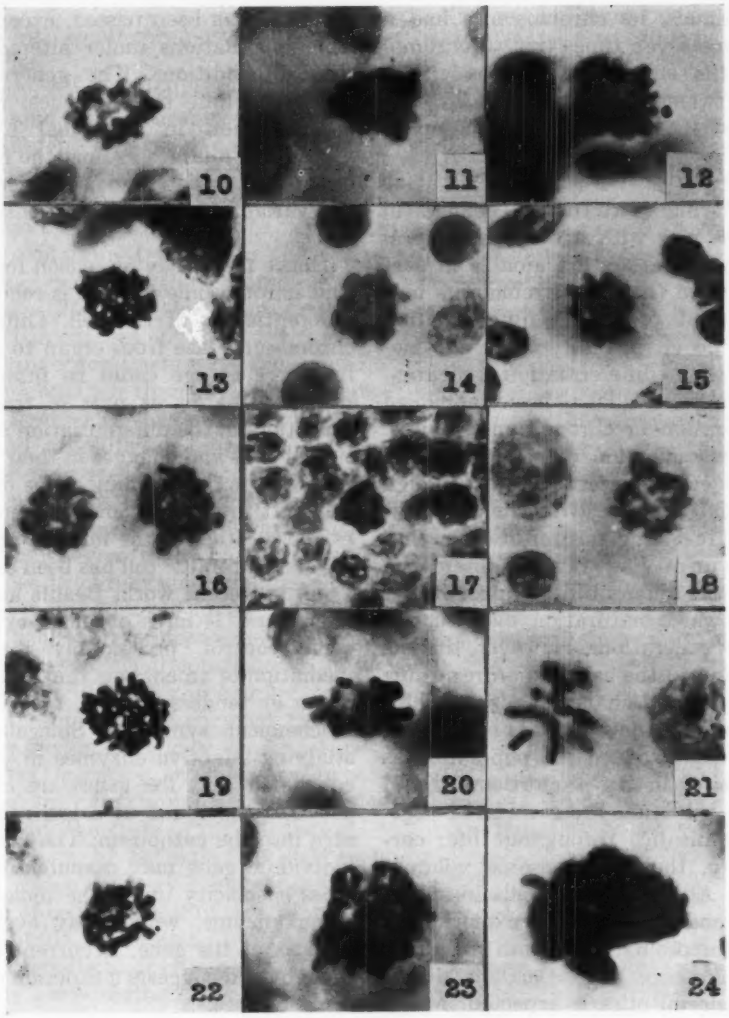


FIG. 9. Variation of average chromosome volume with age in liver epithelium.



FIGS. 10–24. PHOTOMICROGRAPHS OF RAT MITOSES, ×1200. FROM ACETOCARMINE SQUASHES.

FIG. 10. Epidermis of newborn male.
FIG. 11. Lung of embryo male.
FIG. 12. Lung of female no. 387, 901 days old.
FIG. 13. Epithelium of small intestine in newborn male.
FIG. 14. Small intestine of male no. 999, 1011 days old.
FIG. 15. Lymph node of 21 day old male.
FIG. 16. Spleen of newborn male.
FIG. 17. Thymus of embryo male.
FIG. 18. Thymus of newborn male.
FIG. 19. Kidney of newborn female.
FIG. 20. Kidney of 21 day old female.
FIG. 21. Kidney of female no. 478, 1058 days old.
FIG. 22. Liver of newborn male.
FIG. 23. Liver of 21 day old male.
FIG. 24. Liver of male no. 999, 1011 days old.

the old animals, its chromosomes had a mean volume seven times that of chromosomes in the embryonic thymus and a maximum twenty-seven times as large as the smallest set of thymus chromosomes.

Discussion

The differing patterns of change in chromosome size with age in the several organs and tissues are explainable in part if it is assumed that a cell remaining in a given state of functional differentiation will suffer no change in size of chromosomes, but that a differentiation or modulation occurring in a cell may be accompanied by an alteration in chromosome volume. Cowdry's classification of cells is helpful (6). The vegetative intermitotics, although undifferentiated, agree with the fully differentiated reverting postmitotics in that both are in unvarying states of differentiation, while the differentiating intermitotics progress toward maturation over successive mitotic generations. However, the latter, according to the assumption regarding differentiation and change in size of chromosomes, should show changes in chromosome volume, provided the population as a whole shifts in its proportions. Basal cells of the epidermis are considered vegetative intermitotics throughout life; correspondingly, their chromosome volumes vary little. Although stem cells in spleen and lymph nodes are vegetative intermitotics, a chromosomal variation resulting from the presence of descendant differentiating intermitotics is expected. Many late embryonic cell types are differentiating intermitotics, and on this basis change in chromosome size near birth should be present in most tissues. Intestinal epithelium may belong to this class or to the reverting postmitotics, among which (in the adult) Cowdry (6) names cells of liver, kidney, adrenal, and lung. Dawson (7) has also pointed out that fully differentiated liver cells engage in mitosis. Accordingly, there should be little variation in average chromosome volume in these organs, once the transitional period of differentiation in early life has been passed, except for possible modulations under altered environmental conditions. The general lack of change in lung chromosomes, resembling the situation in epidermal basal cells, should not militate against the correctness of the assumption made so much as should the variability of liver chromosomes with age.

Hence there may be reason for the view that chromosome volume is related to the differentiation of the cell. Differences in chromosome size from organ to organ and from age to age could be interpreted as responses to, or as part of the chain of causation in, the differentiation or modulation of cells and changes in their functions. But what is the meaning of the direction of the shift in chromosome volume?

The position of the nucleus as the leading element in the cell has been emphasized again by recent work. Beadle and his collaborators (1) have obtained evidence for genic control, presumably through the mediation of an enzyme that the gene produces or renders specific, of each step in biochemical syntheses. Spiegelman (11), studying adaptive enzymes in yeasts, has concluded that the genes are continually producing enzymes at a low rate for passage into the cytoplasm. The view that an individual gene may manufacture, or impress specificity upon, the molecules of a given enzyme, which may even be free replicas of the gene, is current in genetic thought and suggests a function of somatic chromosomes.

Secondly, there is a relation of a sort between the size of chromosomes and the overall enzymatic activity of the cells of an organ, as well as between chromosome volume and overall concentration of the B vitamins known or thought to be involved, as parts of coenzymes, in enzyme systems (2, 3). Thus, the mammalian liver, noted for its enzymatic activity and vitamin content, has relatively large chromosomes. The cells are also large, however, so that for each unit volume of chromosomal substance there may be more cytoplasm than

in cells with small chromosomes and small cell bodies.

Thirdly, Mirsky, Pollister, and Ris (10) have found that chromosomes isolated from different cell types consist of three substances in variable proportions: desoxyribose nucleic acid, histone or protamine, and a more complex and perhaps varying protein containing tryptophan and apparently equivalent to the chromosomin of Stedman (12). They found progressively higher percentages of the tryptophan-protein in chromosomes of fish erythrocytes, mammalian thymocytes, and mammalian liver cells. Differences in proportions and absolute amounts of the constituents may well underlie differences in size of chromosomes; it is in this light, not forgetting the possibility of variations in coiling and degree of hydration, that the differences in chromosome volume in this material may be looked upon.

The likelihood therefore arises that some or all of the chemical constituents of the chromosomes may vary in amount in relation to the quantity of enzymes manufactured or given specificity by the genes; this latter quantity should vary in accordance with functional activity, as determined by the state of differentiation.

Hence it is to be expected that such changes as senility may bring about in the function of cells could, if of sufficient overall magnitude, be detected by their reflection in altered size of chromosomes by the relatively gross method described. Of the six tissues studied in old age, only the liver epithelium and the epidermis showed significant differences in chromosome size from the size at 3 months. However, it is not certain that these differences are restricted to the latter end of life, as data from middle life are lacking. There is also the possibility that cells capable of mitosis in old animals are cells not yet affected by senility.

Summary

Metaphasic chromosome volume in acetocarmine smears varied from organ to organ (cell type to cell type) and from age to age in 44 Wistar albino rats. The variability among the organs was least in the embryos and greatest in the old animals. There were roughly three patterns of change with age: Chromosome size varied little in epidermis and nonepithelial cells of the lung; a rise in chromosome size at birth, followed by a fall in youth and a lower level in maturity, was found in small intestine epithelium, lymph node, and spleen; an increase from the embryonic volume to a larger size soon after birth and maintained or augmented in maturity and old age, occurred in chromosomes of kidney and liver. It appeared that chromosome volume was more likely to change when the cell was differentiating or modulating, and that it would shift in accordance with quantitative changes in chromosomal functions.

The data did not give clear indications of important alterations of chromosome size in senility.

References

1. Beadle, G. W.: Biochemical Genetics. *Chem. Rev., 37:* 15–96, 1945.
2. Biesele, J. J.: A Relation Between Chromosome Size and B Vitamin Content of Rat Organs. *Am. Naturalist, 78:* 380–382, 1944.
3. Biesele, J. J.: Chromosome Size in Normal Rat Organs in Relation to B Vitamins, Ribonucleic Acid, and Nuclear Volume. *Cancer Research, 4:* 529–539, 1944.
4. Biesele, J. J., and Cowdry, E. V.: Chromosomal Changes in Epidermal Carcinogenesis. *J. Nat. Cancer Inst., 4:* 373–384, 1944.
5. Biesele, J. J., Poyner, H., and Painter, T. S.: *Nuclear Phenomena in Mouse Cancers.* University of Texas Publication No. 4243, Austin, 1942.
6. Cowdry, E. V.: Ch. 24, Ageing of Individual Cells, in *Problems of Ageing.* Williams & Wilkins Co., Baltimore, 1942, second edition.
7. Dawson, A. B.: Cell Division in Relation to Differentiation. *Growth, Supplement No. 2,* 91–107, 1940.
8. Goldschmidt, R., and Fischer, A.: Chromosomenstudien an Carcinomzellen in vitro. *Ztschr. f. Krebsforsch., 30:* 281–285, 1929.
9. Ludford, R. J.: The Behaviour of the Malignant and Non-malignant Cells of Transplantable Tumours in Tissue Cultures. *Arch. f. exper. Zellforsch., 14:* 42–55, 1933.

10. Mirsky, A. E., Pollister, A. W., and Ris, Hans: The Chemical Composition of Chromosomes. *Genetics, 31:* 224–225, 1946.
11. Spiegelman, S.: The Physiology and Genetic Significance of Enzymatic Adaptation. *Ann. Missouri Bot. Garden, 32:* 139–163, 1945.
12. Stedman, E.: The Chemistry of Cell Nuclei. *Edinburgh M. J., 51:* 353–366, 1944.

Submitted for publication June 28, 1946

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Some Chemical Changes in the Human Thoracic Aorta Accompanying the Aging Process

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CHEMICAL DETERMINATIONS OF ELASTIN, COLLAGEN, AND CREATINE IN THE HUMAN THORACIC AORTA WERE MADE BY DR. MYERS AND MR. LANG TO DETERMINE THE EFFECT OF THE AGING PROCESS ON ELASTIC AND CONNECTIVE TISSUE, AND SMOOTH MUSCLE. EIGHTY-THREE AORTAS WERE ANALYZED, THE AGE RANGE OF THE PERSONS FROM WHOM THEY WERE REMOVED AT AUTOPSY BEING 15 TO 88 YEARS. THE CHANGES OBSERVED IN THE MEAN VALUES WERE IN ACCORD WITH THE CONCEPT, BASED ON HISTOLOGIC OBSERVATION, THAT ELASTIN AND MUSCLE DECREASE AND COLLAGEN INCREASES WITH AGE.

IT HAS been assumed on the basis of histologic evidence that the aging process in blood vessels is associated with some decrease in the elastic tissue and a somewhat similar increase in the connective tissue. The suggestion for the present investigation came from a report by Karsner (1) covering a histologic study of the changes in the aortic media in hypertension. Karsner states: "The progressive widening of the spaces between the elastic fibers must be due to an increase in collagenous tissue or muscle or both. To estimate this quantitatively on the basis of microscopic examination is unsatisfactory, and accurate determination must await the development of chemical methods." At the time our study was undertaken (with the cooperation of Dr. H. E. Alburn) a satisfactory method for the estimation of elastin was not available, but a considerable number of estimations of collagen (2), creatine, water, fat, and electrolytes were made on aortic tissue. After the study had been in progress for some time, Lowry, Gilligan, and Katersky (3) described methods for the quantitative estimation of both elastin and collagen which seemed especially suited to the problem we had in mind. The present brief report deals only with this phase of the study, plus an estimate of the smooth muscle on the basis of the creatine content.

The aortas employed in the chemical analyses made were obtained during routine postmortem examinations at the Institute of Pathology, Western Reserve University and University Hospitals, and the Pathological Laboratory of the Cleveland City Hospital through the cooperation of Dr. Howard T. Karsner. The thoracic aorta was used for the analyses. At the time of autopsy the sample was placed in a special bottle, tightly corked, and stored in a refrigerator until analysis could be made, this being done with as little delay as possible (within 48 hours).

METHODS

The adventitia was easily stripped from the aorta and discarded. The remaining tissue (intima and media) was then cut into small pieces and mixed, this being done in a refrigerator. Samples of this material were employed for the determinations of moisture, elastin, collagen, and creatine. One-half gram was used for the determination of elastin and collagen, which determination was carried out as described by Lowry, Gilligan, and Katersky (3). A similar amount of aortic tissue was used for the creatine estimation, which was done as previously described (4).

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The work on this paper was done at the department of biochemistry of the School of Medicine, Western Reserve University, in Cleveland, Ohio.

Results

The data obtained are summarized in tables 1 and 2. The cases have been divided arbitrarily into five groups covering spans of fifteen years, and without regard to pathologic diagnoses. Fifteen-year age groups were used because the number and distribution of cases seemed inadequate to arrange the cases in decades. Unfortunately the tables include no information on individuals in the first decade and a half of life. We are indebted to Dr. Huldah Bancroft, of the Department of Hygiene and Bacteriology, for assistance in the statistical analysis of the data.

Table 2. Creatine Content of the Human Thoracic Aorta

(29 cases divided into 15 year age spans)

	Age in Years	Number Analyzed	Mean Water Content (per cent)	Mean Creatine Content (wet wt.) (mg. per cent)
1	15–29	4	74.5	90
2	30–44	4	77.0	83
3	45–59	10	77.3	76
4	60–74	10	74.8	74
5	80	1	72.3	54

It will be noted in table 1 that the moisture content of the tissue appears to increase slightly up to the age of 59, and subsequently falls off sharply after 60 years of age. As age advances there appears to be a definite decline in the mean elastin content, with a leveling off at the age of about 45 years. The mean findings for creatine, derived presumably from the smooth muscle (table 2), are quite similar. The process in the case of the collagen is the

Table 1. Elastin and Collagen Content of the Human Thoracic Aorta

(83 cases divided into 15 year spans)

	Age in Years	Number Analyzed	Mean Water Content	Elastin			Collagen		
				Wet Wt. Mean	Dry Weight Range	Dry Weight Mean and Standard Error	Wet Wt. Mean	Dry Weight Range	Dry Weight Mean and Standard Error
			per cent	per cent	per cent	per cent	per cent	per cent	per cent
1	15–29	5	74.7	10.85	22–27	37.4 ± 4.8	4.15	12–20	15.4 ± 1.4
2	30–44	16	76.5	7.85	23–27	37.4 ± 1.0	3.68	13–18	15.5 ± 0.4
3	45–59	29	76.7	6.77	21–37	28.8 ± 0.9	4.13	12–24	17.4 ± 0.5
4	60–74	36	71.8	6.76	21–40	26.8 ± 0.9	4.57	14–24	18.1 ± 0.4
5	75–88	7	72.2	6.79	20–36	26.6 ± 2.2	5.03	16–24	19.1 ± 1.0

reverse of this, the mean content remaining relatively constant up to about the age of 45, and then increasing slowly through the remaining years of life.

The highest value for elastin, 47.4 per cent, dry weight, was found in the aorta of an individual 15 years of age, and the lowest, 20.0 per cent, in an individual 83 years of age. Conversely, the lowest collagen, 11.8 per cent, was found at the age of 45, and the highest, 24.3 per cent, in an individual aged 88.

The question may properly be asked: Do the mean values present a correct picture of the aging process? Additional data are presented in table 1 giving the range of values and the standard error for elastin and collagen in the different age groups. It will be noted that the range of values is comparatively large, and if one were merely to look at this scattering of figures without further attempts to analyze the data it would not appear that age had a significant influence on the values. However, the trend line for elastin shows a significant downward trend, decreasing at the rate of 3 per cent every fifteen years. The trend line for collagen shows a slight but not significant increase of 1 per cent every fifteen years. After our work was completed several papers appeared by Hass (5, 6, 7, 8), who has given considerable attention to elastic tissue and especially to the elastin of the aorta. Employing the method of Lowry, Gilligan, and Katersky, Hass analyzed a series of 21 human aortas, from persons aged 10 days to 77 years, and found that the amount of elastin recovered varied from 28.9 to 42.4 per cent (average 37.9 per cent) dry weight. From these data Hass concluded: "There is no relation between the age of the aorta and the percentage of the vessel in the form of elastic tissue. It is apparent that in the average case an increase in the dimensions of the aorta is accompanied by a parallel increase in the amount of the elastic tissue. In individual cases this is not true, presumably because of undue increases in the amount of collagen in the intima or the media." We noted this same scattering of values, observing in our larger series an even wider range of elastin content, from 20.0 to 47.4 per cent dry weight, and probably would have been led to the same conclusion if we had not calculated the mean values for the different age groups. However, the changes observed in the mean values for the different age groups are in harmony with the popular concept, based on histologic observation, that the elastin decreases and the collagen content increases with age.

Summary

Determinations of elastin, collagen and creatine have been carried out on human aortas from autopsy cases, the age range being 15 to 88 years. Although there is considerable scattering of figures, the aging process appears to have a definite influence on the mean values obtained. The highest figures for elastin and creatine (presumably smooth muscle) are found in early life. These gradually decline until about the fifth decade and then remain relatively constant. At about this time the collagen begins to rise and continues to rise slowly through the remaining years of life.

References

1. Karsner, H. T.: Thickness of Aortic Media in Hypertension. *Tr. A. Am. Physicians, 53:* 54–59, 1938.
2. Spencer, H. C., Morgulis, S., Wilder, V. M.: A Micromethod for the Determination of Gelatin and a Study of the Collagen Content of Muscles from Normal and Dystrophic Rabbits. *J. Biol. Chem., 120:* 257–266, 1937.
3. Lowry, O. H., Gilligan, D. R., and Katersky, E. M.: Determination of Collagen and Elastin in Tissues, with Results Obtained in Various Normal Tissues from Different Species. *J. Biol. Chem., 139:* 795–804, 1941.
4. Linegar, C. R., Frost, T. T., and Myers, V. C.: Variation in Creatine Content of Human Cardiac and Voluntary Muscle at Autopsy. *Arch. Int. Med., 61:* 430–450, 1938.
5. Hass, G. M.: Elastic Tissue; Description of Method for Isolation of Elastic Tissue. *Arch. Path., 34:* 807–819, 1942.

6. Hass, G. M.: Elastic Tissue; Study of Elasticity and Tensile Strength of Elastic Tissue Isolated from Human Aorta. *Arch. Path., 34:* 971–981, 1942.
7. Hass, G. M.: Elastic Tissue; Relations Between Structure of Aging Aorta and Properties of Isolated Aortic Elastic Tissue. *Arch. Path., 35:* 29–45, 1943.
8. Hass, G. M.: Studies of Cartilage; Morphologic and Chemical Analysis of Aging Human Costal Cartilage. *Arch. Path., 35:* 275–284, 1943.

Submitted for publication Jan. 15, 1946

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The Effect of Yeast Nucleic Acid on the Survival Time of 600 Day Old Albino Mice

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THE INVESTIGATION OF THE EFFECT OF NUTRITIONAL FACTORS ON THE PROCESS OF AGING HAS ONLY RECENTLY BEEN GIVEN ATTENTION. IN THIS PAPER, DR. GARDNER REPORTS ON THE INCREASE WHICH YEAST NUCLEIC ACID PRODUCES IN THE LIFE SPAN OF 600 DAY OLD ALBINO MICE, AND CONTRASTS HIS RESULTS WITH THOSE OF AN EARLIER INVESTIGATOR WHO ADMINISTERED BOTH YEAST AND THYMUS NUCLEIC ACID IN FAR LARGER AMOUNTS TO MICE FROM BIRTH. DR. GARDNER DISCUSSES THREE POSSIBLE EXPLANATIONS FOR THE INCREASE IN LONGEVITY PRODUCED BY NUCLEIC ACIDS: MAINTENANCE OF A HIGH NUCLEOCYTOPLASMIC RATIO IN THE CELLS, OXIDATION OF INGESTED NUCLEIC ACIDS IN PLACE OF CELL NUCLEIC ACIDS, AND STIMULATION OF LEUKOCYTIC ACTIVITY.

THE importance of nucleic acids in cells in regard to longevity was early claimed by Minot (1). Yeast, or ribose nucleic acid is found in the cytoplasm, and thymus, or desoxyribose nucleic acid in the nucleus of animal cells (2). Until recently it was thought that yeast nucleic acid was found only in plant cells, and thymus nucleic acid, only in animal cells. The concentration of nucleic acids in cells is quite large in many cases. The cytoplasm of rye embryo cells contains 3 per cent (3), yeast cells contain 5–10 per cent (4), and the pancreas, up to 10 per cent (5) nucleic acid of the dry weight.

Wherever there is cell growth (6) or cell division there is a high concentration of nucleic acid, as shown by spectrum absorption measurements (7). Minot (1) observed that as long as the ratio of nuclear material to cytoplasm was high, cells exhibited all of the characteristics of young cells. Robertson and his co-workers carried on extensive investigations on the effect of various nucleic acids on growth and longevity. Preliminary investigations showed that growth was coincident with an increase of nuclear material (8). A method was developed for the measurement of the nucleocytoplasmic ratio by estimating guanine (9). It was found that as tissues grew older, the nucleocytoplasmic ratio decreased. This was found to be the case in wheat (10), the organs of sheep (11), and the organs of white mice (12). Robertson attempted to slow down the fall of the nucleocytoplasmic ratio by feeding large amounts of nucleic acids to his experimental animals (13). This, in effect, increased the survival time of his animals, and large increases of the mean life span were obtained as compared with the controls. The increase in the mean life span was attributed to a decrease in the rate of decline of the nucleocytoplasmic ratio or the promotion of postadolescent growth (14). Robertson's work will be discussed more fully later.

It has been shown that most ingested yeast nucleic acid is oxidized in the body (15). Sometimes retention exceeds three or four days (16) with only 14–30 per cent accounted for by acid excretion. The rate of turnover in rabbits was found to vary from organ to organ and was highest in the muscles (16). The turnover rate was higher in the cytoplasm than in the nucleus. Tracer phosphorus showed a two-thirds turnover in fifty days. The nucleus was found to be the stable element in the cell, and the nucleic acids, the stabilizing agent. The rate of nucleic acid synthesis was highest during growth (18). Tracer

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This paper was presented before the Division of Biological Chemistry at the Atlantic City meeting of the American Chemical Society in April, 1946.

Dr. Charles N. Frey of the Fleischmann Laboratories supplied the yeast nucleic acid used in the experiments reported on in this paper.

experiments using isotopic nitrogen showed that nucleoproteins could not utilize purines nor pyrimidines for synthesis (19) but probably were able to utilize nucleic acids. Using radioactive phosphorus it was observed that there is a slow and steady turnover of thymonucleic and ribonucleic acids in nongrowing liver, but a rapid turnover in growing, regenerating liver, the yeast nucleic (ribo) acid having a greater rate of turnover than the thymonucleic acid (20). It was suggested that ribonucleic acid was necessary for protein synthesis (20). This supports Robertson's hypothesis that nucleic acids promote growth by affecting the nucleocytoplasmic ratio, and thus affect the aging rate.

Robertson's work on the effect of nucleic acids on longevity has been neglected, probably on the assumption that the more recently acquired knowledge of vitamins and the mineral elements in nutrition invalidates earlier work (21). However, this contention is not justified by an examination of the diets of Robertson's animals. They were nutritionally adequate according to modern standards. Therefore it is considered desirable to reexamine and place on a practical basis some of Robertson's work and modify it in the light of modern advances in the field of nutrition.

Up till now the investigation of nutritional factors for animals and man has been almost wholly confined to the growth and health aspects in early life. The problem of aging has only recently been emphasized. Any nutritional factor that would materially increase the average life of older animals would be of interest because of its possible application to man.

Materials and Methods

In my experiment, 600-day old mice were used since mice are beginning to get old at that age.

On the basis of commercial practicability, only yeast nucleic acid can be utilized. Robertson (13) used such large quantities (25 mg. per mouse per day, or about 55 gm. for an adult human being) that they were not practical from a pharmaceutical standpoint. He based these amounts on his hypothesis of excess ingested nucleic acid being necessary to affect the nucleocytoplasmic ratio. However, on the basis of two other just as probable hypotheses for the mode of action of yeast nucleic acid, to be described later, only 2.5 mg. per mouse per day were used in my experiments. The corresponding amount for human beings, 5.5 gm., is entirely practical for clinical testing on aging people.

Seventy-two 600 day old female albino mice were divided into two groups of equal appearance in regard to health, weight, and vitality, one group to serve as controls. Thirty-one 600 day old male albino mice were similarly divided into two groups, 15 to be used for control purposes and 16 for treatment. The mice were all caged separately in clean, dry cages and fed small Purina Dog Chow Checkers ad libitum. Water containing thiamin (vitamin B_1) was given ad libitum to both controls and treated mice. Purina Dog Chow Checkers have been reported to be deficient in this vitamin (22).

The approximate analysis of the yeast nucleic acid used (sample P-36, 3A-872, 10-4-43) was: solids—90–95 per cent; nitrogen—15.17–15.95 per cent (dry basis); phosphorus—8.78–9.4 per cent (dry basis); biuret test—negative. The yeast nucleic acid was a stable powder, slowly soluble in water. It was administered in water solution at the rate of 2.5 mg. per mouse per day.

Results

Table 1 contains the data on the length of life of all mice used in the experiment. The treated mice retained vitality and vigor longer than the controls. Also, the treated mice did not exhibit a noticeable loss of weight before death as the controls did. Fewer of the treated mice went blind before death than did the controls. In all respects, the mice treated with the nucleic acid appeared healthier and exhibited greater activity than the controls.

Whereas the mice were 600 days old at the beginning of my experiment, Robertson fed his mice from birth to death. However for the purpose of comparison, the percentage survivals at different periods were recalculated from Robertson's data (13) on a 600 day basis for mice receiving both yeast nucleic acid and thymus nucleic acid. Table 2 summarizes these calculations.

An examination of table 2 shows that the strains of mice used by Robertson and in the present investigation had different vitality curves. However, the significant increase of percentage survivals at different age levels indicates a real improvement with the use of nucleic acids.

A comparison of the average duration of life obtained by Robertson, who fed nucleic acid from birth, and that obtained in the present investigation in which old mice were used, would seem to favor Robertson's procedure. However on recalculating Robertson's survival data, which he published in complete form, and using mice from his experimental data that survived until the 600 day level, it is seen that the large improvement noted by Robertson is the result of early ingestion of nucleic acids. The improvement obtained in the later periods by Robertson compares remarkably well with that obtained in the present

Table 1. Data on Length of Life of All Mice Tested

Each treated mouse received 2.5 mg. of yeast nucleic acid per day. Length of life is reported in days.

	Males		Females	
	Controls	Treated	Controls	Treated
1	610	608	609	611
2	612	613	629	625
3	613	616	630	635
4	617	621	635	640
5	621	644	640	648
6	635	675	642	648
7	636	692	642	648
8	666	728	646	650
9	682	740	650	655
10	698	744	667	670
11	723	787	667	681
12	782	866	669	682
13	840	913	671	695
14	894	968	677	704
15	962	995	683	720
16	—	1,030	684	734
17			687	740
18			690	755
19			694	768
20			700	782
21			700	788
22			707	793
23			715	801
24			723	814
25			725	835
26			735	845
27			748	850
28			752	865
29			783	890
30			785	902
31			788	915
32			836	935
33			874	955
34			930	980
35			945	992
36			1,015	1,007
Mean Durations of Life and Probable Errors of the Mean				
	706 ±20	765 ±25	721 ±10	774 ±14

TABLE 2. MORTALITY STATISTICS ON MICE RECEIVING NUCLEIC ACIDS
C = Controls T = Treated

Days	Robertson's Investigation						Present Investigation			
	Males*		Females*		Males†		Males‡		Females‡	
	C	T	C	T	C	T	C	T	C	T
600	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
650	81.1	80.0	73.5	95.6	77.8	73.7	53.3	68.8	75.0	77.7
700	50.0	55.0	52.7	78.2	50.0	68.4	33.3	56.2	44.4	63.9
750	18.7	45.0	36.9	60.9	38.9	47.3	26.7	37.5	25.0	52.8
800	12.5	35.0	20.9	39.1	22.2	36.8	20.0	31.2	13.9	38.9
850	6.3	26.5	5.5	26.1	11.2	36.8	13.3	31.2	11.1	25.0
900	6.3	20.0	5.5	13.0	5.5	21.0	6.7	25.0	8.3	19.4
950	6.3	10.1	0.0	4.3	5.5	15.7	6.7	18.8	2.8	11.1
1,000	0.0	5.0		0.0	5.5	5.2	0.0	6.3	2.8	2.8
1,050		5.0			0.0	5.2		0.0	0.0	0.0
1,100		0.0				0.0				

* Mice received thymus nucleic acid corresponding to 0.5 gm. per day of fresh thymus tissue six days a week.

† Mice received 25 mg. of yeast nucleic acid per day for six days a week.

‡ The mice in the present investigation received 2.5 mg. of yeast nucleic acid per day for seven days a week.

work. Table 3 significantly points this out.

An examination of table 3 shows that the lengthening of the life span by feeding nucleic acids is above experimental error and is not dependent upon, nor invalidated by, work performed before the more recent acquisition of knowledge concerning vitamins and mineral metabolism. There is a slight difference between the increase obtained by thymus and by yeast nucleic acids. This may be the result of a difference in digestibility. Fortunately the only one

TABLE 3. MEAN DURATION OF LIFE AND THE PROBABLE ERRORS OF THE MEAN OF MICE RECEIVING NUCLEIC ACIDS FROM BIRTH AND FROM THE 600 DAY LEVEL

	Nucleic Acid from Birth (Robertson)		600 Day Levels			
			Robertson's Recalculations		Present Investigations	
	Males	Females	Males	Females	Males	Famales
Controls	610 ± 18	610 ± 18	703 ± 13	700 ± 13		
Treated with thymonucleic acid	687 ± 17	714 ± 18	758 ± 19	767 ± 14		
% Increase	12.6	17.0	7.8	9.5		
Controls	609 ± 16		726 ± 15		706 ± 20	721 ± 10
Treated with yeast nucleic acid	706 ± 21		777 ± 23		765 ± 25	774 ± 14
% Increase	15.8		7.0		8.4	7.4

which can be produced in commercial quantities, yeast nucleic acid, results in a significant lengthening of the life span. It is evident that treatment with nucleic acids is beneficial at both early and later periods of life, and after the usually accepted growth period has been completed. The improvement in vitality and consequent increase in longevity may hold true for human beings as well as for mice.

Discussion

The work of Robertson and his coworkers on nucleic acids was based on the hypothesis (8-a, 13) that the feeding of large quantities of nucleic acids (55 gm. on an adult human being basis) would result in postadolescent growth, and would tend to lessen the rate of decrease of the nucleocytoplasmic ratio in cells. Thus the cells would retain longer the characteristics of youth, and the individual would have a longer life span. Robertson proved his thesis of postadolescent growth and a longer life span, but recent work (15, 20) tends to show that the nucleic acids are metabolized and probably used in more parts of the cell than in the preservation of the nucleus alone.

In the course of these later investigations two other hypotheses were developed which may partially or wholly explain the increase in longevity that results from the feeding of yeast nucleic acid. The fact that only one tenth of the nucleic acid used by Robertson materially increased the survival values for albino mice partially invalidated Robertson's thesis that the nucleic acid is used only as a food material for growth. Also, the fact that yeast nucleic acid, which is found not in the nucleus but in the cytoplasm, increases the life span as well as thymus nucleic acid, which is found in the nucleus, would seem to indicate other modes of operation of nucleic acids than the effect on the nucleocytoplasmic ratio alone.

One hypothesis that would partially fit into Robertson's nutrient thesis is that there are two ways of maintaining a high nucleocytoplasmic ratio. Robertson stressed the growth of the nucleus, but the other way is by slowing down the metabolism of the nucleus by giving to the cell, nucleic acids that can be utilized in metabolism without destroying the nucleus or cytoplasm. Thus the cells live longer at a higher energy level. The ingested nucleic acids would then have a sparing action on the cell nucleic acids and be oxidized in place of them. This would be analogous to but not necessarily the same as the sparing action of vitamin E on vitamin A (23). To contrast Robertson's theory with the newer hypothesis, Robertson emphasized anabolism, while the sparing action hypothesis stresses the slowing down of the catabolism of the essential nucleic acids.

The second hypothesis succeeding Robertson's is based on the experimental fact that in strains of mice in which the females live longer than the males, the females have a higher white blood count, while in other strains, those mice having the highest white blood count live the longest, strain for strain, and females over males respectively (24). This has also been suggested as the reason that women live longer than men. The injection of solutions of sodium yeast nucleinate has been used for some time to stimulate leukocytic growth and activity (25). Therefore, if the daily ingestion of small quantities of yeast nucleic acid should stimulate the white blood cells and tend to keep them at a slightly higher level than they would be otherwise, the organism would be able to fight better and to recover more quickly from pathogenic substances than it ordinarily would. It is a known fact that the leukocytic response to infection is slower in old people than in young people. The decrease in resistance to infection is undoubtedly a major factor in aging, and just as the anti-reticular cytotoxic serum (ARCS) developed in Russia (26) is claimed to increase the resistance to infection and to promote a longer, healthier life, so nucleic acids may stimu-

late in a similar manner. This hypothesis is submitted in spite of the fact that Robertson failed to find any increase in leukocytic activity in his human subjects (28). However, his subjects ingested the nucleic acids for only a few weeks, and it may take several months to obtain an increase in activity. The lengthening of the life span of mice is not apparent until after about fifty days of treatment, a period which would correspond to about five years in man. Therefore the increase in leukocytic activity may be slow.

Nucleic acids in relatively large amounts have been eaten for several weeks without ill effects. Robertson and his co-workers found that 15 gm. per day of yeast nucleic acid, and also other nucleic acids in varying quantities, had no effect on the basal metabolism (27) and urinary excretion of man (28). I have eaten 5 gm. of yeast nucleic acid per day for weeks without any ill effects. (Yeast nucleic acid is sour to the taste, and it was found convenient to dissolve the nucleic acid in approximately one third its weight of sodium bicarbonate in half a glass of water. In this form it is palatable. The total dosage was divided into two parts and taken at morning and at night, so as to keep the metabolism balanced. Yeast sodium nucleinate can also be used for animals in place of the acid.)

As Robertson tested with three times the amounts I have suggested for use, there is no reason known at the present time for fearing to use yeast nucleic acid freely for veterinary experimental purposes on cats, dogs, and various other mammalian pets for extending their life spans, as well as for experimental therapy on aging men and women for the same purpose. Fortunately, a recently published method may make it possible to detect any decrease in the aging rate within a period of about two years (32). If found beneficial, nucleic acid may not be advocated much before middle life, but the fact that it can aid at later ages is indicative of the body's capacity to respond to proper stimuli. There is some evidence that old mice (over 700 days of age) also respond to yeast nucleic acid (29).

The development of factors which will effectively slow down degenerative changes and which may be used like vitamins is a major objective of gerontotherapeutic work. At the present time only two such materials may be obtained in the United States—yeast nucleic acid and methyl testosterone (or testosterone propionate). Testosterone has shown evidence of affecting degenerative changes to some extent, (30), and it has recently been highly publicized in a popular book describing its effects (31).

The use of both yeast nucleic acid and methyl testosterone together, and the development and use in America of Russia's anti-reticular cytotoxic serum in conjunction with the other two agents have not been investigated at the present time.

The effect of yeast nucleic acid on the human leukocytic level will be reported on later.

Summary

1. The effect of yeast nucleic acid on the longevity of 600 day old albino mice was investigated.

2. The average life of the male albino mice was increased 8.4 per cent and that of the female mice, 7.4 per cent by the daily ingestion of 2.5 mg. of yeast nucleic acid, added to an already adequate diet.

3. The investigation was correlated with the work of Robertson and his co-workers on the observed increase in longevity of albino mice obtained by the dietary addition of large amounts of yeast and other nucleic acids of various origins.

4. Two hypotheses to explain this increased longevity were discussed in addition to Robertson's theory of a nucleocytoplasmic ratio level upheld by an excess of nutrient nucleic acid. One hypothesis suggested that the ingested nucleic acid may be metabolized in place of the cell

nucleic acids; the other hypothesis suggested that the nucleic acid may increase leukocytic levels and that consequently a greater resistance to infection may be maintained.

References

1. Minot, C. S., *The Problem of Age, Growth, and Death.* G. P. Putnam's Sons, New York, 1908.
2. *a.* Mirsky, A. E.: Ch. I. Chromosomes and Nucleoproteins, in Nord, F. F., and Werkman, C. H.: *Advances in Enzymology, 3:* 1–34, 1943; *b.* Davidson, J. N., and Waymouth, C.: Tissue Nucleic Acids. I. Ribonucleic Acids and Nucleotides in Embryonic and Adult Tissues. *Biochem. J., 38:* 39–50, 1944.
3. Feulgen, R., Behrens, M., and Mahdihassan, S.: Isolation and Identification of the Nucleic Acids of Plant Cell Nuclei. *Ztschr. f. physiol. Chem., 246:* 203–211, 1937.
4. Delaporte, B.: The Nucleic Acids of Yeast and Their Localization, *Rev. gén. botan., 51:* 449–482, 1939.
5. Jorpes, E.: Analysis of Pancreatic Nucleic Acids. *Acta. med. Scandinav., 68:* 503–573, 1928.
6. Caspersson, T., and Thorell, B.: Nucleic Acids in Embryonic Tissues. *Chromosoma, 2:* 132–154, 1941.
7. Caspersson, T., and Schultz, J.: Pentose Nucleotides in the Cytoplasm of Growing Tissues. *Nature, 143:* 602–603, 1939.
8. *a.* Robertson, T. B.: *The Chemical Basis of Growth and Senescence.* Monographs on Experimental Biology, J. B. Lippincott Co., Philadelphia, 1923; *b.* Robertson, T. B.: The Duration of Life. *Australian Assoc. Adv. Sc., 18:* 863–882, 1926.
9. Robertson, T. B.: Colorimetric Method of Determining Guanine: Application to Determination of Nucleo-cytoplasmic Ratios. *Australian J. Exper. Biol. & M. Sc., 6:* 33–58, 1929.
10. Huelin, F. E.: Nucleo-cytoplasmic Ratios in Plant Tissues. *Australian J. Exper. Biol. & M. Sc., 6:* 59–63, 1929.
11. Robertson, T. B., and Dawbarn, M. C.: Preliminary Communication on the Influence of Age of the Animal upon the Nucleic Acid and Coagulable Nitrogen Content of the Tissues of Sheep. *Australian J. Exper. Biol. & M. Sc., 6:* 261–275, 1929.
12. Dawbarn, M. C.: The Nucleo-cytoplasmic Ratio of the White Mouse and its Variation with Age. *Australian J. Exper. Biol. & M. Sc., 9:* 213–225, 1931.
13. Robertson, T. B.: Influence of Nucleic Acids of Various Origin upon the Growth and Longevity of the White Mouse, *Australian J. Exper. Biol. & M. Sc., 5:* 47–67, 1928.
14. Robertson, T. B., Marston, H. R., and Walters, J. W.: The Influence of Starvation and of Intermittent Starvation Plus Nucleic Acid on the Growth and Longevity of the White Mouse. *Australian J. Exper. Biol. & M. Sc., 12:* 33–45, 1934.
15. Wilson, D. W.: Studies in Pyrimidine Metabolism. *J. Biol. Chem., 56:* 215–227, 1923.
16. Givens, M. H., and Hunter, A.: Experiments upon the Fate of Ingested Sodium Nucleate in the Human Subject. *J. Biol. Chem., 23:* 299–309, 1915.
17. Hahn, L., and Hevesy, G.: Turnover Rate of Nucleic Acid. *Nature, 145:* 549–550, 1940.
18. Brues, A. M., Tracy, M. M., and Cohn, W. E.: Relation Between Nucleic Acid and Growth. *Science, 95:* 558–560, 1942.
19. Plentl, A. A., and Schoenheimer, R.: Studies in the Metabolism of Purines and Pyrimidines by Means of Isotopic Nitrogen. *J. Biol. Chem., 153:* 203–217, 1944.
20. Brues, A. M., Tracy, M. M., and Cohn, W. E.: Nucleic Acids of Rat Liver and Hepatoma. Their Metabolic Turnover in Relation to Growth. *J. Biol. Chem., 155:* 619–633, 1944.
21. Private communication from Dr. C. M. McCay.
22. Griffiths, W. J., Jr.: Absence of Audiogenic Seizures in Wild Norway and Alexandrine Rats. *Science, 99:* 62–63, 1944.
23. Hickman, K. C. D., Kaley, M. W., and Harris, P. L.: Covitamin Studies. III. The Sparing Equivalence of Tocopherols and Mode of Action. *J. Biol. Chem., 152:* 321–328, 1944.
24. Reich, C., and Dunning, W. F.: Leucocyte Level and Longevity in Rats. *Science, 93:* 429–430, 1941.
25. *Merck Index.* Merck & Co., Rahway, N. J., 1940, fifth ed., pp. 388, 515.
26. Bogomolets, A. A.: Anti-reticular Cytotoxic Serum as a Means of Pathogenic Therapy. *Am. Rev. Soviet Med., 1:* 101–112, 1943; Marchuk, P. D.: A Method of Preparing and Preserving Anti-reticular Cytotoxic Serum. *Ibid., 1:* 113–123; Linberg, B. E.: Anti-reticular Cytotoxic Serotherapy of Fractures and War Wounds. *Ibid., 1:* 124–127.
27. Hicks, C. S.. Basal Metabolism of Man on a Diet Rich in Nucleic Acid. *Australian J. Exper. Biol. & M. Sc., 4:* 151–154, 1927.
28. Robertson, T. B., Hicks, C. S., and Marston, H. R.: Comparison of the Utilization of Nucleic Acids of Animal and Vegetable Origin. *Australian J. Exper. Biol. & M. Sc., 4:* 125–150, 1927.
29. Gardner, T. S., and Forbes, F. B.: The Effect of Sodium Thiocyanate and Yeast Nucleic Acid on the Survival Time of 700 Day Old

Albino Mice. J. GERONTOLOGY, *1:* 453–456, 1946.
30. Silberberg, M., and Silberberg, R.: Effects of Hormones on the Skeleton of Mice, Guinea Pigs and Rats. *Endocrinology, 29:* 475–482, 1941.
31. De Kruif, P.: *The Male Hormone.* Harcourt, Brace and Co., New York, 1945.
32. Bernstein, F., and Bernstein, M.: Law of Physiologic Aging as Derived from Long Range Data on Refraction of the Human Eye. *Arch. Ophth., 34:* 378–388, 1945.

Submitted for publication June 12, 1946

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The Effect of Sodium Thiocyanate and Yeast Nucleic Acid on the Survival Time of 700 Day Old Albino Mice

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IT HAS BEEN FOUND THAT YEAST NUCLEIC ACID CAN COUNTERACT THE DECREASE IN SURVIVAL TIME OF MICE PRODUCED BY THYROID ACCELERATORS, SUCH AS THYROID EXTRACT. HOWEVER, THE EFFECT ON SURVIVAL TIME OF NUCLEIC ACID USED IN CONJUNCTION WITH THYROID INHIBITORS, SUCH AS SODIUM THIOCYANATE, HAS NOT PREVIOUSLY BEEN INVESTIGATED. DR. GARDNER AND MR. FORBES FOUND THAT WHILE YEAST NUCLEIC ACID CANNOT OVERCOME THE CUMULATIVE TOXIC EFFECTS OF THIOCYANATE INGESTED DAILY, IT DOES EXTEND THE LIFE SPAN OF MICE FED INTERMITTENT DOSES OF THIOCYANATE.

ROBERTSON and his co-workers (1) found that yeast nucleic acid fed to mice from birth increased the mean duration of life. The effect of nucleic acids on the longevity of mice has been summarized in a preceding paper, pp. 445–452 of this issue (2). It was shown in this preceding paper that yeast nucleic acid increased the mean survival of old albino mice, even though fed at one tenth the levels used by Robertson.

It was found by Robertson that thyroid accelerators, such as thyroid extract, decreased the mean duration of life of mice, but that if nucleic acid were added to the diet of the mice the life span rose to normal; and that if the thyroid extract was removed from the diet, the mean duration of life increased (3).

The effect on the survival time of mice of thyroid inhibitors administered in conjunction with nucleic acid has not previously been investigated. Yeast nucleic acid has been reduced to a practical basis for use in work on aging (2). Thyroid inhibitors have recently become important in the control of hypertension (4), as counteragents for benzedrine (5), and as substances exerting an influence on increased survival values at low pressures (6) and decreased survival values on implosive decompression (7). Thiourea and the thiocyanates are the most commonly used thyroid inhibitors. Thiocyanate is of especial interest in the problem of aging because of its effect on cholesterol metabolism. Malisoff has shown that a high level of ingested thiocyanates will prevent the deposition of cholesterol in the walls of the blood vessels of dogs (8) and rabbits (9) when these animals are fed an excessive amount of cholesterol. The relation between the deposition of cholesterol, and arteriosclerosis and atherosclerosis is of vital interest to all investigators of the aging process (10).

The cumulative effects of thiocyanate therapy are so pronounced and serious that we considered it desirable to determine whether or not yeast nucleic acid might act as a counteragent to thyroid inhibitors just as it does for thyroid accelerators (3). Another objective of the investigation was to determine if intermittent doses of thiocyanate had the same detrimental effect as daily ingestion of the material.

MATERIALS AND METHODS

Albino mice at an initial age level of 700 days were used in the experiments. The treated mice were fed 2.5 mg. of yeast nucleic acid (2) per day, and 4.5×10^{-5} gm. of sodium thiocyanate per day in the first part of the experiment (table 1), while in the second part of the experiment this amount of sodium thiocyanate (4.5×10^{-5}

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Francis B. Forbes entered the chemical research field at the conclusion of his junior year at North Carolina State College. He spent twelve years with the Tennessee Eastman Corporation, working on wood distillation, alcohol denaturants, and yarn research. He is now in the process of completing his B.S. degree, which he will receive from State College, Johnson City, Tennessee in May, 1947. His chief interests are along the lines of nutritional, biochemical, and pharmaceutical research.

This paper was presented before the Division of Biological Chemistry at the Atlantic City meeting of the American Chemical Society in April, 1946.

Dr. Charles N. Frey of the Fleischmann Laboratories supplied the yeast nucleic acid used in the experiments reported on in this paper.

gm.) was administered once a week (table 2).

The daily dosage would produce in a week a cumulative action equivalent to the recommended dosage for insomnia, that is, 0.6–0.7 gm. (11). However this amount is much less than that used for the reduction of hypertension (4).

No differentiation was made between male and female mice. Thirty-one mice were used as controls, and the same number were treated, as shown in table 1. After sixty-two days, the survivors were divided into equal groups for the second experiment (table 2).

Results

The daily ingestion of sodium thiocyanate and nucleic acid was highly toxic (table 1). After sixty-two days only 48.6 per cent of the mice receiving both yeast nucleic acid and sodium thiocyanate were still alive, while 74.2 per cent of the controls survived.

The mice who died while taking the thiocyanate-nucleic acid treatment exhibited nervousness, and there was swelling of the thyroid glands.

The mice that survived the 62-day period were then equally divided, both as to treated and control groups, for the second experiment. The intermittent ingestion of a small quantity of thiocyanate was found to have little or no effect on the beneficial aspects of yeast nucleic acid. An immediate improvement was observed after cessation of the daily thiocyanate treatment, and the survival time of mice treated intermittently with thiocyanate was gradually extended (table 3).

Table 1. Daily Thiocyanate Treatment

The treated mice were fed both 2.5 mg. yeast nucleic acid and 4.5×10^{-5} gm. of sodium thiocyanate per mouse per day. Thirty-one mice were used as controls, and 31 were treated. Only the age at death is reported.

Treated			Controls		
No.	Age in Days	Sex	No.	Age in Days	Sex
1	703	M	1	705	F
2	721	F	2	705	F
3	721	M	3	707	F
4	730	F	4	729	M
5	730	M	5	734	M
6	737	F	6	742	F
7	737	M	7	759	F
8	741	M	Nos. 8–31 inclusive survived the 762 day period.		
9	745	F			
10	745	F			
11	746	M			
12	749	F			
13	757	F			
14	760	F			
15	762	F			
16	762	M			
Nos. 17–31 inclusive survived the 762 day period.					

No further attempt was made to analyze the results statistically.

Discussion

It is evident that thiocyanates are toxic if ingested daily. Although they have been used to decrease hypertension, it has also been observed that they lower the basal metabolism ratio (4). In spite of the fact that large doses of thiocyanates tend to prevent arteriosclerosis and atherosclerosis by preventing the deposition of cholesterol in the walls of blood vessels, they are too dangerous to be employed for this purpose. Although a decrease in cholesterol-type degenerative diseases would tend to prolong life, the toxic effects of the agent used to obtain this decrease would most certainly decrease survival values. However, it appears that intermittent doses of thiocyanate have little, if any, effect on survival times when used in conjunction with yeast nucleic acid. Sodium thiocyanate has often been used to prevent insomnia (11), and persons taking it over a period of years have shown no ill effects if the material has not been taken too often.

Yeast nucleic acid cannot overcome the cumulative toxic effects of daily ingestion of sodium thiocyanate, but the nucleic acid does begin to be beneficial after cessation of daily use of thiocyanate. It is evident that mice over 750 days old can be benefited insofar as survival time is concerned by the daily ingestion of yeast nucleic acid. This observation increases the weight of the data reported on in the preceding paper (2).

The results obtained by the use of thyroid inhibitors are in contrast to those obtained with thyroid accelerators (3). Thus, yeast nucleic acid can bring to normal survival values those animals taking thyroid extract, but cannot do so for those on sodium thiocyanate. These points should be carefully observed in the use of both thyroid accelerators and yeast nucleic acid.

Table 2. Intermittent Thiocyanate Treatment

The treated mice were fed 2.5 mg. yeast nucleic acid per day per mouse, and 4.5×10^{-5} gm. sodium thiocyanate per mouse in one dose per week. The "Sex" column also indicates the grouping of the mouse in the first experiment—that is, FC = Female, Control; FT = Female, Treated.

Treated			Controls		
No.	Age in Days	Sex	No.	Age in Days	Sex
1	764	FC	1	764	FC
2	779	FC	2	779	MC
3	781	MT	3	783	MT
4	791	FC	4	784	FC
5	792	FC	5	788	MC
6	799	MC	6	793	FC
7	803	FT	7	802	FC
8	814	FT	8	804	MC
9	860	MC	9	811	MC
10	874	FC	10	827	MT
11	902	FT	11	843	MC
12–15 lived through the 902 day period, at which time the experiment was abandoned.			12	844	FT
			13	860	FT
			Nos. 14 and 15 were the only two to survive the 902 day period for the controls.		

Summary

1. The effect of sodium thiocyanate and yeast nucleic acid on the survival time of 700 day old albino mice was investigated.

2. Daily administration of a small quantity of sodium thiocyanate (4.5×10^{-5} gm.) in conjunction with yeast nucleic acid (2.5 mg.) decreased the survival time of treated mice over that observed for the controls.

Table 3. Percentage of Mice Surviving Intermittent Thiocyanate Treatment

Days	Treated	Controls
762	100.0%	100.0%
800	60.0	60.0
850	46.7	26.6
900	33.3	13.3
902	26.7	13.3

The controls received neither nucleic acid nor thiocyanate.

3. Intermittent administration of a small quantity of sodium thiocyanate (4.5×10^{-5} gm. once a week) in conjunction with yeast nucleic acid (2.5 mg. per day) produced increased survival values as compared with the controls.

4. The increase in survival time of mice treated with intermittent doses of sodium thiocyanate and yeast nucleic acid is undoubtedly due to the beneficial effects of the nucleic acid rather than to any effects obtained from the thiocyanate. This conclusion is based on previous experiments with animals receiving yeast nucleic acid (2).

References

1. Robertson, T. B.: Influence of Nucleic Acids of Various Origin upon the Growth and Longevity of the White Mouse. *Australian J. Exper. Biol. & M. Sc., 5:* 47–67, 1928.
2. Gardner, T. S.: The Effect of Yeast Nucleic Acid on the Longevity of 600 Day Old Albino Mice. J. GERONTOLOGY, *1:* 445–452, 1946.
3. *a.* Robertson, T. B.: Influence of Thyroid Alone and of Thyroid Administered Together with Nucleic Acids upon the Growth and Longevity of the White Mouse. *Australian J. Exper. Biol. & M. Sc., 5:* 69–88, 1928; *b,* Robertson, T. B., Dawbarn, M. C., Walters, J. W., and Wilson, J. D. O.: The Influence of Continuous Administration of Vegetable Nucleic Acid and the Intermittent Administration of Thyroid upon Growth and Longevity (of the White Mouse). *Australian J. Exper. Biol. & M. Sc., 11:* 219–235, 1933.
4. *a* Caviness, V. S., Umphlet, T. L., and Royster, C. L.: Blood Pressure and Thiocyanates. *Am. J. M. Sc., 204:* 688–697, 1942; *b.* Potter, E. B.: Acute Goiter Due to Cyanate Therapy. *J.A.M.A., 124:* 568–570, 1944.
5. Gardner, T. S.: Chemical Controls of Nervous Tension Used by Graduate Students. *J. Tennessee Acad. Sc., 16:* 290–292, 1941.
6. Gordon, A. S., Goldsmith, E. D., and Charipper, H. A.: Thiourea and Resistance to Low Atmospheric Pressures ("High Altitudes"). *Science, 99:* 104–105, 1944.
7. Gardner, T. S., and Forbes, F. B.: The Effect of Thiourea on Mice Undergoing an Abrupt Reduction in External Atmospheric Pressure. *J. Aviation Med., 16:* 99–100, 1945.
8. Malisoff, W. M.: *The Span of Life,* J. B. Lippincott Company, Philadelphia, 1937.
9. Malisoff, W. M.: Prevention of Atherosclerosis. I. Administration of Potassium Thiocyanate. *Proc. Soc. Exp. Biol. & Med., 35:* 356–358, 1936.
10. *Biological Symposia, XI, Aging and Degenerative Diseases.* The Jaques Cattell Press, Lancaster, Pennsylvania, 1945.
11. Bancroft, W. D., and Rutzler, J. E., Jr.: The Agglomeration Theory of Sleep. *Proc. Nat. Acad. Sc., 19:* 73–78, 1933.

Submitted for publication June 12, 1946

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Characteristics of Compulsory Health Insurance

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AFTER DISCUSSING IN DETAIL THE GERMAN AND ENGLISH HEALTH INSURANCE SYSTEMS IN RECENT ISSUES OF THE JOURNAL OF GERONTOLOGY, DR. WILSON HERE COMPARES THESE SYSTEMS WITH THOSE OF OTHER COUNTRIES AND DISCUSSES THE PROBLEMS ALL OF THEM HAVE FACED AND THE SOLUTIONS WHICH HAVE BEEN ATTEMPTED. THE PROBLEMS INCLUDE: LIBERAL BENEFITS FROM THE BEGINNING OR LOW BENEFITS GRADUALLY RAISED; INCLUSIVE COVERAGE FROM THE OUTSET OR GRADUAL EXTENSION OF COVERAGE; FLAT-RATE BENEFITS OR BENEFITS BASED ON ACTUAL WAGE LOSS; MALINGERING; AND LAY INTERFERENCE WITH PHYSICIANS.

NOT only was the German health insurance system the first to be inaugurated, but it may be considered typical of most of the forty other systems which have been implemented since 1883. Any deviation from the German form may be attributed to the difference in maturity between the German and later systems, a desire to take advantage of any errors the Germans had made, or special conditions existing in the country introducing the system.

It was pointed out in my article on the German insurance system in the April issue of the JOURNAL OF GERONTOLOGY that the German system was set up, not because of the demands of the workers, but because of the political ambitions of Bismarck. The same thing happened in England. Indeed, Lloyd George admitted in 1938 that "the need of the Liberals to takes votes from the growing Labor Party had more to do with the adoption of health insurance than the need of the poor for medical care."

England and Germany are only two of many countries in which the origin of health insurance was political rather than sociologic. Indeed, a political origin for health insurance was so common that a noted sociologist once remarked that "sickness insurance is the politician's panacea for social unrest." In 1934 an American writer claimed that although health insurance "is always urged in the interest of the underpaid workers, these have never been responsible for, nor even highly favorable to, its enactment. Instead, laborers have demanded that wages be sufficiently high to enable the recipients to pay their own medical expenses. In no country, have laborers led the demand for sickness insurance." However both the A.F. of L. and the C.I.O. have come out in favor of the Wagner-Murray-Dingell Bill.

Furthermore, it is of interest to note that "no system owes its introduction primarily to any socialist or labor party." On the contrary, the early systems—as in Germany and Britain—were introduced in order to defeat such radical organizations. But they were not successful. When the Social Democrats in Germany and the Labor Party in England realized that the system was popular with the workers, they lost no time in joining their political opponents in sponsoring the measure, so that the passage of the legislation was not of any lasting advantage, politically speaking, to the original sponsors. Parenthetically, it should be noted that the Social Democrats and the Labor Party are in the ascendency in their respective countries today. Since both major parties here have gone on record as approving the adoption of health insurance legislation, its adoption would not be a triumph for either party.

It will be remembered that the original German law covered only about 10 per cent of the population, but that by 1937 at least two-thirds of the population was included in the system. The other early systems followed the German example and gradually extended coverage. In England,

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less than half of the working force were covered by the system in 1912, but thirty years later, 90 per cent were. Up until the late 1920's, the maturity of a health insurance system could be estimated by the proportion of coverage of the laboring population. In only a very few instances did the introduction of the system to cover part of the workers not result in a rather rapid spread to include practically all workers.

Extension of coverage was so universal that the more recent systems have started out with a fairly inclusive coverage. This was what the French did in 1928–1930, as did the countries created by the Versailles Treaty. However, there were drawbacks to inclusive coverage. The administrative difficulties it involved will be discussed later. There was also a psychological problem. In the systems where the introduction of coverage was gradual, the included workers felt they were favored, and preened themselves accordingly. The workers who were included later felt that they had achieved a desired goal. On the other hand, if a system was imposed on all the workers at the same time, it seemed to assume the form of another unwanted tax rather than a desired privilege.

This happened in France. All, or practically all, of the workers were included in the system, which began operations in 1930; but in 1936, the insurance authority reported that one-third of the eligible workers had not paid the dues and had failed, therefore, to qualify for the benefits. The French workers obviously did not consider membership in the health insurance system as much of a privilege as did the English or the German workers—undoubtedly because in France the system was imposed on the workers as a completed whole; they had no sense of participation or accomplishment connected with it. The attitude was different in England, where the coverage was introduced gradually, and the National Health Insurance System became the workers' pride. The Wagner-Murray-Dingell Bill provides for rather complete coverage from the outset.

Another phase of the problem of coverage is whether the benefits should be high from the beginning, or low and increase gradually. In Germany, the benefits provided by the original law were extremely meager, but competition between the Kassen liberalized them. The same thing happened in England. Increased benefits brought with them higher costs, but the workers who had had the lower benefits were willing to pay the higher tax. It was different in France. A completed program was imposed on the workers in one fell swoop—and the workers did not like the taxes. The Wagner-Murray-Dingell Bill provides for rather liberal benefits from the start.

The question of adjustment of benefits deserves closer examination. The main cash benefits provided by the German system were the wage-loss benefit for temporary disability, and the disability or invalidity benefit which partially indemnified the worker for wage loss due to a more protracted illness. The disability benefit was usually about half the amount of the wage-loss benefit. It has been pointed out that the wage-loss benefit was liberalized as to amount—originally it was half the basic wage but later it was often three-fourths—and as to duration of payment. Originally, the full benefit was paid for only three months and then cut in half; later, it was customary to pay the full benefit for twenty-six weeks.

The British noted this liberalization of benefits, and saw, too, that the costs of the German system increased more than proportionately. They realized that with more generous benefits there was more and more malingering. In order to avoid this, they decided to base the benefit not on the wage but on what they called a "minimum floor of protection." Therefore they decided on a flat rate benefit, which should be paid to all insured workers. This was not outstandingly successful in mitigating malingering. In 1938, a survey showed that 15 per cent of those who were receiving benefits were able to work.

Moreover, the flat rate benefit encouraged malingering among the lower paid workers. For instance, when the women's benefit was fixed as 12s. in 1920, it approximated the net wage earned by married women after the fee they had to pay for the care of their children was deducted. It is not surprising that the number of claims entered by married women more than doubled in the period 1921–1927. Again in 1935, when the disablement benefit was 41 per cent of the average wage for boys and 58 per cent of the girls, the claim rate among young people was unusually high. Furthermore, the basic rate for men moved ever upwards.

It is not surprising then that the success of the English system did not seem so outstanding that other countries wanted to imitate it. In fact, only the Irish Free State and certain Swiss cantons decided to give the flat rate benefit to all workers. France, realizing that it was extremely hard to determine a wage scale for agricultural workers, compromised and gave a flat rate, modified for dependents, to agricultural workers, but paid other workers a benefit based on the wage received.

All other countries with insurance systems followed the German example and based the cash benefit on the wage. This does not mean that they paid the same proportion or paid it for the same period. They did not. The German benefit was paid from the fourth day of illness. Bulgaria and Portugal do not require any waiting period. Australia insists on a week. In Chile, the benefit is retroactive after a five day waiting period. In France, the waiting period varies with the number of dependents. In Russia, it depends on the worker's union record.

The wage loss benefit is paid for varying lengths of time. Norway pays it for thirty-nine weeks. Chile pays the full wage for one week, then half the wage for another week, and a quarter of the wage from the beginning of the third week of illness until the beginning of the seventh month, when, under certain conditions, the full wage again becomes payable. In Russia, the benefit paid to a trade unionist is increased after a month. However, these are unusual cases, and the majority of countries pay the wage-loss benefit for six months.

Most of the countries also follow the German example and pay a benefit which lies somewhere between one-half and two-thirds of the basic wage. However, there are variations. The industrious Dutch have found that it is feasible to pay 80 per cent of the basic wage, whereas the Mexican worker gets only half that proportion. These ratios reflect the industry and wealth in the respective countries. In France and the Union of South Africa, the amount of the benefit varies with the number of dependents; in Russia, it depends on the worker's status in the union. Again, these provisions are the result of special conditions in the countries concerned. The Russian authorities want to strengthen the power of the unions, and in France and South Africa, it is important to increase the population and, therefore, to hold out all sorts of inducements to make the support of large families easy.

This same motive is seen in the liberal maternity benefit given in France. The French mother receives a lump sum, the wage-loss benefit for twelve weeks, a nursing benefit—a small cash payment—for five months, and the medical benefit during pregnancy and after confinement. This should be compared with the meager

English benefit, which consists only of a lump sum payment of £2. The pregnant English woman is not allowed free medical care within four weeks of confinement. However in most systems the usual maternity benefit consists of a small lump sum, medical care for the woman, and a wage-loss benefit if she is a worker. This type of maternity benefit is a part of practically all the more recent laws.

On the other hand, the funeral benefit is found in only about half of the most modern legislation. The funeral benefit is a life insurance policy, the face of which is for a sum usually equal to between twenty and forty weeks' compensation. When it was dropped from the English bill, at the insistence of the industrial insurance companies, Britain became the first country with a health insurance law which did not contain a funeral benefit provision. Since then, this provision has been omitted from many laws.

Ten years ago there was great variation in the medical benefits, and less than full coverage of the population could have been explained by any one of a number of reasons, such as immaturity of the system and special objections on the part of those in power to certain types of benefits. Today, however, there is such a decided trend for complete coverage in practically all countries that any deviation therefrom is a measure of lack of facilities and not unwillingness on the part of the authorities to give all types of service. Of course, in South Africa, where there is only one doctor for every 4,000–6,300 inhabitants, and in certain parts of South America, where any medical service would have to be furnished by travelling clinics, really adequate service would be impossible to guarantee. In other parts of the world where doctors are more numerous, the greatest variation in the medical service will be found in the dental and nursing benefits. This variation is also due to inadequacy of personnel.

Of course it is true that conditions within a given country may determine the types of medical benefits on which the most emphasis is placed. For instance, in England, the system of public hospitals makes it unnecessary to stress the hospital benefit. In Chile, the high morbidity rate is, in large part, the result of venereal, tubercular, and cardiovascular diseases, all of which can be helped by early discovery. That is why the periodic examination takes an important place among the medical benefits. The Chilean authorities are so determined to minimize these diseases that a worker who is afflicted with one of them is penalized if he does not take advantage of the "preventive rest period" when it is prescribed.

With the increase in importance of the medical benefit, there has come a change in the attitude of insurance authorities and physicians towards each other. In the early days of the German system, the doctors were sympathetic and often gave their services free of charge. It was not long, however, before feuds developed. The Kassen directors accused the physicians, who were paid on a fee-for-service basis, of over-practice and false certification of claims. Moreover, they refused to permit certain well qualified physicians to enter insurance practice. The doctors resented this lay interference and loss of professional prestige. The feuds became more bitter, and did not end until the doctors were regimented under a professional organization after the accession of the Nazis.

The English tried to profit by the German experience. In England any qualified physician was permitted to "go on the panel," and physicians were given a choice between a fee-for-service or a capitation basis of remuneration. However they were encouraged to select the capitation basis, which eliminated charges of over-practice. Although the administration of the medical benefits was entirely separated from the cash benefit, friction between the doctors and the Societies which administered the cash benefits was not eradicated. There was still the dispute over certification. There existed the same old cycle which occurred in every country with

health insurance: The benefits were increased, either through competition or political pressure; malingering increased; costs went up; the insurance authorities blamed the doctors; the doctors resented "lay interference."

The French authorities decided to avoid all this bickering, so they let the physicians draw up the medical benefit. Instead of giving service in kind, they decided to refund to the worker a part of any moneys he had expended for medical attention. The benefit was based on a fixed schedule, but physicians did not have to abide by it. Through this arrangement, the worker was supposed to pay only about one-fifth of the medical costs; in reality, he paid about one-half. This system of refund was not successful in preventing disputes between the insurance *caisses* and the doctors. One French commentator charged that the method "facilitates the greatest amount of fraud and dishonest dealing." Because malingering was rife, about half of the urban claims certified by physicians were rechecked by employees of the insurance societies. That did not improve the relations between the doctors and the health insurance system.

Not only did the doctors object to lay interference, but many also felt that "the dual attitude of policeman and physician introduces an atmosphere of hostility and suspicion into the relation of patient and practitioner and makes diagnosis and treatment difficult and unsatisfactory." Moreover, "the great amount of time required for police work often makes proper attention to legitimate medical work impossible." If the vast amount of paper work required of the doctors is considered as well as the many demands on their time by malingerers, it is not surprising that serious questions have been raised as to whether insurance medicine can, on the whole, ever be first rate.

In addition to the disputes over certification, which are found in all countries with insurance systems, and the uncertainty of many physicians over the quality of care the workers receive (Ernest Bevin called it "a tragedy of incompetence"), two other situations have irked physicians. The first is lay interference with such a purely professional matter as prescribing medicines; the other has to do with fixing the physicians' fees.

In England, the Ministry of Health had the druggists make out a formulary of cheap drugs, which the Ministry tried to force physicians to prescribe. If he did not cooperate, the Minister of Health could disqualify a doctor from insurance practice. No wonder the Lord Chief Justice wrote of "the despotism of the Minister of Health!" Again, in Chile, the treatment of patients suffering from certain diseases is prescribed by edict, and the doctors who do not conform are penalized.

In Germany, the doctors complained because the insurance authorities were apt to engage the poorer doctors—that is, those whom they could get for the least money. There have been disputes over fees in other countries. In New Zealand, the doctors objected to treating well-to-do-patients for the same low fee they were paid for the low-paid worker. In fact, in 1940 conditions became so bad that each worker had to make an individual contract with a doctor. However, this "proved unacceptable to the majority of the medical profession," and New Zealand went back to a fee-for-service basis. In Norway, insurance funds have found it so difficult to fix fees acceptable to physicians that they have periodically resorted to the French refund system, but there has been constant dissension between insurance administrators and physicians.

Conditions in all countries have become better if and when the supervision of the physicians has been entrusted to a committee of physicians. This happened in Germany when the K.V.D. (Krankenkassenaerztliche Vereinigung Deutschlands) was put in charge of all medical decisions. English doctors were more content when it was decided that all questions of a medical nature should be decided by mem-

bers of the profession. However, supervision by the medical profession does not solve the problem of disputes over certification. Until there are a sufficient number of doctors so that the certifying physicians can be entirely separated from the attending physicians, it does not seem probable that complete harmony will exist in any health insurance system.

Turning now to the question of costs, it is found that in practically all health insurance systems, costs have continued to increase with the passage of years. In fact, Czechoslovakia is the only country which has been able to decrease the rate of contribution. In all of the others, costs have risen at varying rates. There are two reasons for this: increased benefits and a higher claim rate. The liberalization of benefits has been discussed already, and it has been intimated that as the benefits approach the full wage, malingering becomes more common. This was at least part of the reason that the German morbidity rate trebled in forty-five years, between 1885 and 1930, and the British rate increased more than 50 per cent from 1921 to 1927. A similar increase in the morbidity rate occurred in other countries with insurance systems.

Thus it is not surprising that the per capita cost in Germany increased sixfold in forty-five years. In England, it doubled by 1927, and in France, where malingering took on the proportions of a public scandal, the cost increased almost 50 per cent in the first five years of the system.

This great increase in cost made the problem of financing the system extremely important. In the early days of the German system, the theory was that the worker himself should bear two-thirds of the cost and the employer the other third, and that governmental participation should be limited to the administrative costs for the central administration. As the costs increased, it was seen that this would impose too great a load on the workers. In fact, in Germany the union leaders were worried lest the worker's insurance tax should becomes so high that he would be unable to pay his union dues. That is why under the edict of 1930, workers and employers were required to share the cost equally. Under the Nazis, more governmental participation was provided.

In Britain, the employer and employee shared the cost almost equally from the first, and the government paid a definite—and appreciable—amount. The contributions, which are on a flat rate basis, have continued to rise for the worker and employer, but the part paid by the government has decreased, relatively if not absolutely.

To generalize, it might be said that the typical health insurance system is supported by a tripartite contribution from the employee, the employer and the government. The proportion of the costs contributed by each varies according to the conditions in each country. For instance, in pre-Nazi Germany, governmental participation was limited to the administrative costs of the central administration; in Russia, the government pays the whole bill. Usually employer and employee pay the same amount, but Romania does not require any employer donation, whereas Peru assesses the employer 6 per cent of the payroll, and then has the employee contribute on the basis of the availability of medical facilities.

Of course, the cost of any health insurance system is contingent, in a great measure, on the efficiency of the administration. In almost all countries with health insurance plans there were voluntary organizations which paid sickness benefits before compulsory health insurance was initiated. These societies became the nucleus for the compulsory insurance administration. Much emphasis has been laid on the fact that there has been an almost universal trend for voluntary systems to become compulsory, but little has been said about the fact that the experience and facilities of the voluntary organizations have assisted materially in simplifying the transition from a system of private medical

care to one of compulsory health insurance. There is no such definite system of voluntary health insurance in the United States which can be relied on for experience and advice.

Once the private insurance societies had become part of the compulsory insurance system, they gained in strength, because of increased membership, and in political prestige. For instance, an English observer wrote in 1941: "It is interesting to contrast the power, the influence and the great wealth of the Approved Societies today with their almost hopeless position before National Health Insurance was introduced." Proof of the political influence of the Approved Societies is the fact that although a Royal Commission reported in 1925 that the administration of the cash benefit by the Societies was inefficient and uneconomic, they were still admistering the benefit twenty years later. Again, it will be remembered that the potential power of the German Kassen was so great that one of the first acts of the Nazis when they came into power was to convert the Kassen into governmental agencies and to use them as implements with which to regiment the German people.

If health insurance is inaugurated here, its implementation will involve the creation of the largest bureaucracy America has ever had. Some experts say that its personnel may well exceed half a million persons. Moreover, these administrators will be strategically placed, in every hamlet, in every corner of every town. What guarantee is there that someday some demagogue will not seize that organization and use it to regiment America?

It is interesting to speculate whether, if the Wagner-Murray-Dingell Bill is passed, the history of health insurance here will parallel that in other countries. There will be fairly complete coverage of almost all workers from the beginning, and the suggested benefits are extremely liberal. Will there be political pressure to make the benefits still more generous? Probably so. In that case, will the morbidity rate in this country increase, just as have the rates in other countries? Undoubtedly, because there will be more malingering here than in those countries where the administration of the benefits is in the hands of the workers themselves. It is estimated that the original costs of the system will be about 6 per cent of the worker's pay check; with increasing benefits and claims, will this ratio rise to 10 or 12 per cent, or more? If it does, will the economy of the country be able to stand it? Only time will tell.

Summary

Health insurance systems have been set up in some forty countries, patterned more or less after the German system, which was the first to be inaugurated. A political origin was common to many. The early systems extended coverage and liberalized benefits gradually; the systems set up more recently have had fairly inclusive coverage and liberal benefits from the start. All systems have had to contend with the same problems—increase in costs, increase in malingering, disputes between insurance authorities and physicians over the certification of claims, and resentment on the part of physicians against lay interference in professional matters.

Submitted for publication March 1, 1946

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The Bible and Old Age

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THAT SCRIPTURAL WRITERS WERE WELL AWARE OF BOTH THE LIABILITIES AND THE ASSETS OF OLD AGE IS THOROUGHLY DOCUMENTED BY MR. GRIFFIN IN THIS STUDY OF SOME OF THE EARLIEST REFERENCES TO OLD AGE WHICH CAN BE FOUND IN CHRISTIAN LITERATURE. MANY OF THE PHYSICAL EFFECTS OF AGING WHICH ARE DESCRIBED, AS WELL AS THE ATTITUDES OF YOUNGER PEOPLE TO THE AGED, ARE SIMILAR TO THOSE RECOGNIZED AS CHARACTERISTIC TODAY. IN FACT, DESPITE THE MODERN BELIEF THAT STUDIED OBSERVATION OF THE PROCESSES OF AGING IS COMPARATIVELY NEW, THERE IS PRACTICALLY NO ASPECT OF SENESCENCE WHICH THE BIBLE DOES NOT TOUCH UPON.

THE title of this article may, at first glance, appear to present an incongruous juxtaposition of subjects, for the notion has gained currency among some groups of social workers that studied observation of the natural process of aging is relatively new. That the Bible constitutes a congeries of documents of undisputed antiquity is universally recognized. Moreover, research demonstrates that the Bible, precisely as a source-book of history, is laden with riches of evidence that cannot reasonably be ignored by students of gerontology. There is scarcely any aspect of senescence which has not been highlighted in one way or another in the course of the Scriptural story. Mention here will be confined to a few of the more provocative illustrations.

Could there for example, be anything better calculated to lend perspective to governmental administrators engaged in the planning of postwar programs of social security than the reading of the Scriptural narrative relating the aftermath of the victory of the army of Judas Macchabeus over the hosts of Nicanor? Subsequent to the account of the number slain and the booty taken it is said succinctly of the triumphant: "They divided amongst them many spoils, giving equal portions to the feeble, the fatherless, and the widows, yea, and the aged also" (1). Incidentally, it may be remarked that the principle of parity emphasized in the distribution of public relief in this instance certainly tends to shatter present day complacency in the measure of social progress achieved!

From the very beginning there is revealed in the ancient writ an alert consciousness of the effects and of the significance of aging. *Genesis*, the first book of the Bible, contains many indications of this sensitiveness to age. In fact, it is replete with genealogies starting with Adam, who, it is said "lived a hundred and thirty years and begot a son to his own image and likeness, and called his name Seth, and the days of Adam after he begot Seth were eight hundred years, and he begot sons

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and daughters, and all the time that Adam lived came to nine hundred and thirty years, and he died" (2). A little later in the annals of generation there is mention of Mathusala, presumably the senior citizen of his day, of whom it is didactically stated: "All the days of Mathusala were nine hundred and sixty nine years, and he died" (3). The annalist gives no intimation that he regards Mathusala's longevity as remarkable.

It may come as a surprise to some readers that the popular idiom referring to a "good old age" is traceable to the early paragraphs of the Bible. Thus, it is recorded that God promised Abram: "Thou shalt go to thy fathers in peace, and be buried in a good old age" (4). The verification of this prediction is likewise mentioned: "The days of Abram's life were one hundred and seventy five years, and decaying he died in a good old age, and after having lived a long time, and being full of days, and was gathered to his people" (5).

The fact that Abraham's 175 years was considered a good old age in his time seems notably significant in view of the multicenturied lives previously given attention. This decided decrease in longevity seems to proceed apace with the advancing history of mankind, for in the writings attributed to Samuel it is said that "Berzellai the Galaadite was of a great age, that is to say, fourscore years old" (6).

In regard to Abraham, moreover, in contrast to prior recordings, it is considered wonderful that a son was born to him "when he was a hundred years old—for at this age was Isaac born." Furthermore Sara, who bore Isaac "in her old age," was fearful that the news would be greeted with incredulity by the community, and cried: "Whosoever shall hear of it will laugh at me—who would believe that Abraham should hear that Sara gave suck to a son, whom she bore to him in his old age?" (7). The exact relation of Sara's age to that of Abraham is, unfortunately, not established.

The patriarchal documents furnish an abundance of testimony manifesting the interest of the people in both the physical degeneration and the mental deterioration of the aged. In the book of *Genesis* there is the pathos-pregnant observation concerning the last days of Isaac, as a prelude to the famous recital about Jacob and Esau: "Now Isaac was old, and his eyes were dim, and he could not see; and he called Esau, his elder son, and said to him: My son?" (8). Loss of visual acuity as an accompanying symptom of declining health is referred to also in the comparable and equally poignant report of Joseph's visit to his dying father, Israel (that is, Jacob), wherein it is related: "After these things, it was told Joseph that his father was sick, and he set out to go to him, taking his two sons Manasses and Ephraim. And it was told the old man: Behold thy son Joseph cometh to thee: and being strengthened he sat up in bed—And when Joseph was come to him—seeing his sons, he said to him: Who are these? He answered: they are my sons—and he said: bring them to me that I may bless them. For Israel's eyes were dim by reason of his great age, and he could not see clearly. And when they were brought to him he kissed them and embraced them . . ." (9).

The other characteristic and chronic ailments of the senium were not overlooked.

While speculation is hazardous, it may well be that the following notation about Asa is the first historical remark relative to gout: "But in the days of his old age he [Asa] was diseased in his feet" (10). In the biographic sketch of David there is apparently an allusion to the sequelae of anemia so commonly discovered in the aged. It is stated simply: "Now King David was old, and advanced in years: and when he was covered with clothes, he was not warm" (11). Nor did the condition of distorted vertebrae escape specific scrutiny, judging at least from the literary climax used to emphasize the cruelty of the King of the Chaldeans: "He had no compassion on young man or maiden, old man or even him that stooped for age—" (12).

The more obvious superficial effects of aging are referred to frequently in the Biblical literature. Job, in his affliction, protests: "My skin is withered and drawn together" (13), and in the mournful prayers of Jeremiah there occurs the witness: "My skin and my flesh he hath made old, he hath broken my bones" (14). Samuel, in his eloquent but somewhat diffuse challenge to the people of Israel, calls attention to his venerable appearance as well as to the unassailable integrity of his career, declaring: "But I am old and greyheaded, and my sons are with you; having then conversed with you from my youth unto this day, behold here I am. Speak of me before the Lord, and before his anointed whether I have taken any man's ox, or ass, if I have wronged any man, if I have oppressed any man, if I have taken a bribe at any man's hand, and I will despise it this day and return it to you. And they said: thou hast not wronged us, nor oppressed us, nor taken ought at any man's hand" (15). The dying David, giving his final charge to Solomon, thus admonishes his son to bring revenge against his old enemy Joab: "Do therefore according to thy wisdom, and let not his hoary head go down to hell in peace" (16). Again, there is the familiar prayer of the Psalter: "Thou hast taught me, O God, from my youth, and unto old age and grey hairs, do not forsake me" (17). The same sentiment is reechoed with a metaphorical application in the words of the prophet acting as the vicar of God, to all Israel: "Even in your old age, I am the same, and to your grey hairs I will carry you" (18).

The general exhaustion and concomitant debility of old age are variously exhibited in the Scriptures. The basic proposition is set forth that "the strength of a man is according to his age" (19). Age, too, as a criterion of ability to serve in the military is mentioned, as in "and the number of them that were of the age that was fit for war, was six and twenty thousand" (20). The official hierarchy instituted by the aged David shows, furthermore, an implied acceptance of full maturity as a prerequisite for prudence in government, in judicial exercises, and in ministerial functions, while simultaneously recognizing the wisdom of retiring from too heavy responsibilities upon reaching real superannuation. It is written: "And David being old and full of days, made Solomon, his son, king over Israel. And he gathered together all the princes of Israel, and the priests and the Levites. And the Levites were numbered from the age of thirty years, and upwards: and there were found of them thirty-eight thousand men. Of these, twenty-four thousand were chosen, and distributed unto the ministry of the house of the Lord: and six thousand were the overseers and judges. Moreover four thousand were porters and as many singers to the Lord with the instruments he had made . . ." (21).

Yet more explicit assertions about the depreciation of stamina in the aged are supplied in other passages. The picture of an enfeebled old person trudging up a roadless hill is utilized as a simile in the maxim: "As the climbing of a sandy way is to the feet of the aged, so is a wife full of tongue to a quiet man" (22). Death "from old age" was presumably the diagnosis in the case of Isaac, of whom it is said: "Being

spent with age, he died" (23), although Noemi uses the same phrase in another connotation when she exclaims: "I am now spent with age and not fit for wedlock" (24). This woman's alertness to the meaning of age is additionally attested by her advice to her two widowed daughters-in-law, who wished to stay with her but whose companionship she chose to forego lest by the delay "you would be old women before you marry" (25).

It may be that the scrivener of antiquity anticipated one of the current concepts as to the causation of arteriosclerosis when he offered the counsel (which might well be that of a contemporary practitioner of psychosomatic medicine): "The joyfulness of the heart is the life of a man—and the joy of man is length of life—drive away sadness from thee—for sadness hath killed many and there is no profit in it. Envy and anger shorten a man's days, and pensiveness will bring old age before the time" (26). In respect to the infirmity of the aged, especially memorable also is the contrast accented in the prophetic words to Jesus to the impetuous Peter: "Amen, amen, I say to thee. When thou wast younger thou didst gird thyself, and didst walk where thou wouldst. But when thou shalt be old, thou shalt stretch forth thy hands, and another shall gird thee, and lead thee whither thou wouldst not."

The underlying fear of total incapacitation in old age is not without expression. There is the prayer of the psalmist: "Cast me not off in the time of old age, when my strength shall fail, do not forsake me" (28). Caleb is considered to have been extraordinarily favored by God because "his strength continued even to his old age, so that he went up to the high places of the land and his children obtained it for an inheritance: that all the children of Israel might see that it is good to obey the holy God" (29). Redolent of pessimism is the understandable apostrophe: "O death, thy sentence is welcome to the man that is in need, and to him whose strength faileth, who is in a decrepit age, and that is in care about all things, and to the distrustful that loseth patience" (30).

Some Biblical explanations would seem to intimate that mental deterioration is almost the inevitable correlative of chronologic senility. Classified in a single category, in one instance at least, are: "the unwise, and foolish and the aged" (31).

Again, Elias rebukes his seniors, who failed to cope with the difficulties proposed by the suffering Job, in like tone: "Then, Elias the son of Barachel the Buzite answered, and said: I am younger in days, and you are more ancient; therefore hanging down my head, I was afraid to show you my opinion. For I hoped that greater age would speak, and that multitude of years would teach wisdom. But—they that are aged are not the wise men, neither do the ancients understand judgment" (32).

The author of *Ecclesiasticus* sets down in his canons of wisdom: "Three sorts my soul hateth, and I am greatly grieved at their life: a poor man that is proud, a rich man that is a liar, an old man that is a fool and doting." Whereupon he proceeds to soliloquize: "The things that thou hast not gathered in thy youth, how shalt thou find them in thy old age? O how comely is judgment for a grey head, and for ancients to know counsel! O how comely is wisdom for the aged, and understanding and counsel to men of honor! Much experience is the crown of old men, and the fear of God is their glory" (33). That the foibles of elderly women were also noted may be inferred from the admonition couched in popular idiom, which St. Paul sent to Timothy: "Avoid foolish and old wives' tales" (34).

But it is not only the liabilities of old age that are exposed. There is much in the Bible calculated to exhibit the accrued assets and grand dignity of the aged. Thus it is laid down as a general principle that "old age is a crown of dignity, when it is found in the ways of justice" (35). In the account of the vision of Jeremias accorded Onias, "There appeared also another man

admirable for age and glory" (36). In glorification of the intrepid young Daniel, who shrewdly unravelled the treacherous plot of the elders who occasioned the condemnation of Susanna, it is said: "Seeing God hath given thee the honour of old age" (37). In the *Psalms* it is sung confidently of the just: "They shall increase in fruitful old age, and shall be well treated that they may show that the Lord God is righteous . . ." (38). In *Proverbs* we are reminded that "a joyful mind maketh age flourishing, a sorrowful spirit drieth up the bones" (39). Even the luminous beauty of a ruddy face enhaloed in an aureole of snowy tresses captured the heart of one ancestral poet, for such he must have been who wrote: "As the lamp shining upon the holy candlestick, so is the beauty of the face in a ripe age" (40). That mere age, devoid of sagacity and virtue, has no lawful claim to reverence is expressed, however, in the text: "Venerable old age is not that of long time, nor counted by the number of years, but the understanding of a man is grey hairs, and a spotless life is old age" (41). Modern science would probably paraphrase the evaluation thus: "There is no necessary parallel between chronologic age and physiologic or psychologic age" (42).

Throughout the Scriptures there is an unvarying insistence upon the debt of respect and assistance which the younger generation owes to the elders. Thus, there is the precept: "Son, support the old age of thy father and grieve him not in his life, and if his understanding fail, have patience with him, and despise him not when thou art in thy strength, for the relieving of the father shall not be forgotten" (43). The most recent books of etiquette do not improve upon the ancient formula: "Rise up before the hoary head, and honor the person of the aged man" (44). Practical is the motive suggested in the exhortation: "Despise not a man in his old age, for we also shall become old" (45).

Some of the most inspiring and realistic dramas that illustrate this phase of traditional morality are found in the Old Testament. Peculiarly appealing, for instance, is the story of Tobias, with its atmosphere of familial solidarity so significant a factor in the psychologic adjustment of the aged. The narrative detailed in the tome titled by his name tells how Tobias, the elder, a man distinguished for his charity, became impoverished and lost his sight at the age of 56. Having prayed God to be delivered to death, he summoned his son and namesake and in a last desperate effort to save the family from total destitution, commissioned him to go to the distant land of the Medes to collect a debt of ten talents of silver, long overdue. The youth, accompanied by an escort (later identified as the angel Raphael), went on the journey and during his travels got married. The ensuing delay tortured the distraught parents, but eventually Tobias returned with his endowed wife, miraculously effected the cure of his father's eyes in the latter's sixtieth year, and settled down in the old homestead with his parents, until his father died at the age of 102 years and his mother shortly afterwards.

The pertinence of the story lies in the reciprocal attitude of loyalty displayed not only between the younger Tobias and his parents but later in relation to his parents-in-law. Full of insight, for example, is the scene graphically depicted following Tobias' departure:

"Then all things being ready—Tobias bade his father and mother farewell.—Now when they were departed his mother began to weep and to say: thou has taken the staff of our old age and sent him away from us. I wish the money for which thou hast sent him, had never been. For our poverty was sufficient for us, that we might account it as riches, that we saw our son. And Tobias said to her: weep not, our son will arrive thither safe, and will return safe to us, and thy eyes shall see him.—At these words his mother ceased weeping, and held her peace" (46).

The human quality of this scene is sup-

plemented by the scene portraying the not untypical state of mind possessing the aged couple when their son fails to return on the day scheduled: "But as Tobias made longer stay upon occasion of the marriage, Tobias, his father, was solicitous, saying: Why thinkest thou, doth my son tarry, or why is he detained there? Is Gabelus (the debtor) dead, thinkest thou, and no man will pay him the money? And he began to be exceedingly sad, both he and his wife with him, and they began both to weep together because their son did not return to them on the day appointed. And his mother wept and was quite disconsolate, and said: Woe is me, my son, why did we send thee to go to a strange country, the light of our eyes, the staff of our old age, the comfort of our life, the hope of our posterity? We having all things together in thee alone, ought not to have let thee go from us. But Tobias said to her: Hold thy peace, and be not troubled, our son is safe . . ." (47).

Finally, the impressive book of Tobias concludes in this fashion: "And it came to pass, that after the death of his mother, Tobias (the younger) departed out of Ninive with his wife, and children and children's children, and returned to his father and mother-in-law. And he found them in health in a good old age, and he took care of them and he closed their eyes, and all the inheritance of Raguel's house came to him and he saw his children's children to the fifth generation—and after he had lived ninety nine years in the fear of the Lord, they buried him" (48).

Another portrayal representative not only of Biblical times but of the perennial position of grandmothers is delineated in the story of Ruth, the childless widowed daughter-in-law of Noemi. Ruth, being married (the second time) to Booz, gave birth to a child, and we are told: "The woman said to Noemi: blessed be the Lord who hath not suffered thy family to want a successor, that his name shall be preserved in Israel. And thou shalt have one to comfort thy soul, and cherish thy old age. For he is born of thy daughter-in-law who loveth thee, and is much better to thee than if thou hadst seven sons. And Noemi taking the child laid it in her bosom and she carried it and was a nurse to it. And the women, her neighbors, congratulating with her said: There is a son born to Noemi . . ." (49).

It is quite possible that the author of the Scriptural aphorism, "A young man according to his way, even when he is old will not depart from it," (50) was subtle enough to have intended a twofold interpretation—namely, that the aged not only manifest both the good and evil manners to which they have become habituated but frequently reveal again in senility a tendency toward some of the indiscretions of youth. Even of Solomon the Wise it was recorded: "When he was old, his heart was turned away by women to follow strange gods"(51). St. Paul seems to have been mindful of the possibilities when he offered his advice to the aged: "Speak the things that become sound doctrine: that the aged men be sober, chaste, prudent, sound in faith, in love, in patience. The aged women in like manner, in holy attire, not false accusers, not given to much wine, teaching well: that they may teach the young women to be wise, to love their husbands, to love their children, to be discreet, chaste, sober, having a care of the house (52)."

It is amply clear that the highest ideals were expected of the sound aged. That such lofty standards were exemplified in the characters of many ancient stalwarts is unquestionable. There is room here but for one illustrious example, in concluding this short study. It is the magnificent account of the heroic Eleazar, who suffered martyrdom by decree of Antiochus because he would not violate the Mosaic law. The record is brief but profoundly moving:

"Eleazar, one of the chief of the scribes, a man advanced in years, and of a comely countenance, was pressed to open his mouth to eat swine's flesh. But he choosing

rather a most glorious death than a hateful life, went forward voluntarily to the torment. And considering in what manner he was come to it, patiently bearing, he determined not to do any unlawful things for the love of life.

"But they that stood by, being moved with false pity, for the old friendship they had with the man, taking him aside, desired that flesh might be brought which it was lawful for him to eat, that he might make as if he had eaten as the king had commanded, of the flesh of the sacrifice, that by so doing he might be delivered from death, and for the sake of their old friendship with the man they did him this courtesy.

"But he began to consider the dignity of his age, and ancient years, and the inherent honour of his grey head, and his good life and conversation from a child: and he answered without delay, according to the ordinance of the holy law made by God, saying that he would rather be sent into the other world. For it doth not become our age saith he, to dissemble: whereby many young persons might think that Eleazar, at the age of four score and ten years, has gone over to the life of the heathens. And so they, through my pretence, and for a little time of a corruptible life, should be deceived, and hereby I should bring a stain and a curse upon my old age. For though for the present time I should be delivered from the punishments of man, yet should I not escape the hand of the Almighty neither alive nor dead. Wherefore by departing manfully out of this life, I shall show myself worthy of my old age; and I shall leave an example of fortitude to young men, if with a ready mind and constancy I suffer an honorable death, for the most venerable and holy laws.

"And having spoken thus, he was forthwith carried to execution (53)."

Summary

The Bible reveals an alert consciousness among the people of its times of the effects and the significance of aging. Such characteristic liabilities of age as failing eyesight, stooping back and shoulders, wrinkled and dry skin, and the tendency to be cold are commented upon. The general infirmity of the aged is referred to. But there are also many references to the happiness that old age may bring if the heart remains young and joyful, and to the assets of dignity, respect, and affection that come with the years if they are earned by wisdom and virtuous character.

References

These references are to the Apocrypha, rather than to the King James version of the Bible.

1. II Macchabees, VIII, 30.
2. Genesis, V, 3–5.
3. Genesis, V, 27.
4. Genesis, XV, 15.
5. Genesis, XXV, 7–8.
6. II Kings, XIX, 31.
7. Genesis, XXI, 2–7.
8. Genesis, XXVII, 1.
9. Genesis, XLVIII, 1–10.
10. III Kings, XV, 23.
11. III Kings, I, 1.
12. II Paralipomenon, XXXVI, 17.
13. Job, VII, 5.
14. Lamentations, III, 4.
15. I Kings, XII, 2–4.
16. III Kings, II, 6.
17. Psalms, LXX, 17–18.
18. Isaiah, XLVI, 4.
19. Judges, VIII, 21.
20. I Paralipomenon, VII, 40.
21. I Paralipomenon, XXIII, 1–5.
22. Ecclesiasticus, XXV. 27.
23. Genesis, XXXV, 29.
24. Ruth, I, 12
25. Ruth, I, 13.
26. Ecclesiasticus, XXX, 13–26.
27. John, XXI, 18.
28. Psalms, LXX, 9.
29. Ecclesiasticus, XLVI, 11
30. Ecclesiasticus, XLI, 3, 4.
31. Ecclesiasticus, XLII, 8.
32. Job, XXXII, 6, 7, 9.
33. Ecclesiasticus, XXV, 3–8.
34. I Timothy, IV, 7.
35. Proverbs, XVI, 31.
36. II Macchabees, XV, 13.
37. Daniel, XIII, 50.
38. Psalms, XLI, 15.

39. Proverbs, XVII, 22.
40. Ecclesiasticus, XXVI, 22.
41. Wisdom, IV, 8, 9.
42. Cf. Lawrence K. Frank, J. GERONTOLOGY, *1:* 1–11, 1946. Also, *Mental Disorders in Later Life, Symposium*, edited by Oscar J. Kaplan, Oxford University Press, New York, 1945.
43. Ecclesiasticus, III, 14, 15.
44. Leviticus, XIX, 12.
45. Ecclesiasticus, VIII, 7.
46. Tobias, V, 22–28.
47. Tobias, X, 1–6.
48. Tobias, XIV; 14–16.
49. Ruth, IV, 14–17.
50. Proverbs, XXII, 6.
51. III Kings, XI, 4.
52. Titus, II, 1–5.
53. II Macchabees, VI, 18–28.

Submitted for publication July 27, 1946

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CURRENT COMMENT

Gerontology in the Renaissance

Nearly four centuries ago, Gabriele Paleotti, an Italian humanist, wrote a treatise entitled "De Bono Senectutis," which means "concerning the blessing of old age." It was published, in Latin, in 1595, translated into Italian in 1597, and printed again in Latin in 1754. Since then the book seems to have fallen into complete oblivion, and has only recently been brought to light by Karl Stern and Thomas Cassirer in the May, 1946 issue of the *American Journal of Psychiatry*.

It is, of course, no surprise to find that during the sixteenth century, the time of the great humanists, there was considerable interest in the problems of old age. The humanists began where the ancient Greek and Latin scholars had stopped, and such famous treatises on old age as that by Cicero must have been exceedingly tempting as a point of departure to a sixteenth century humanist.

But the amazing part of Paleotti's treatise is its modern viewpoint and frequent observations concerning the psychologic adjustments of age, observations accurate according to present-day concepts.

Paleotti deals extensively with the melancholia of many older people, well aware that their mental depressions are more serious than those of any other age group because the aged are deprived of the hope that their discomforts will abate with the mere passing of time.

It is astounding that in discussing depressions Paleotti makes the modern distinction between those causes arising from within the individual (endogenous) and those arising from without (exogenous). Thus he is aware that "occupational therapy, change of environment, and certain other superficial psychotherapeutic methods bring symptomatic relief but do not affect these emotional disturbances at the root." Paleotti says: " 'We agree that these things [music, games, plays, drives, baths, beautiful scenery, etc.] help a good deal in many cases, depending on the nature of the individual case, and that they usually bring comfort . . . yet they do not reach the hidden cause of this sadness, so that when these remedies are discontinued, that intrinsic cause of sadness keeps gnawing at the mind. Thus, in these means, there is no sure hope of restoring the aged or of alleviating sadness.' "

Gabriele Paleotti was not a medical man. He was a jurist, a theologian, and a philosopher, and it appears that "De Bono Senectutis" is the only one of his works not dealing with legal or ecclesiastic problems. It is written in three parts. The first part

The establishment of the JOURNAL OF GERONTOLOGY has been made possible by a grant from the Josiah Macy, Jr., Foundation in support of the editorial office.

The hieroglyphics, "The Beginning of the Book for Transforming an Old Man into a Youth," at the top of this editorial page, are from the Edwin Smith Surgical Papyrus, translated by Professor John Breasted, University of Chicago Press.

is a critical review of the literature, profusely illustrated with quotations from ancient literature. The second part discusses common objections against old age. The third part is devoted to a defense of old age, the gist being that "wisdom, maturity, and a cooling down of certain emotional currents give old age its peculiar form of creativeness unobtainable at other life periods."

Aging Successfully

"If you wish to live long, you must be willing to grow old," says George Lawton, director of the Old Age Counseling Center of New York City, in the May issue of the *Ladies' Home Journal*. There is no secret formula for longevity, and most of the restrictions on activity placed upon older people only make life seem longer by making it duller. It is not how long a person lives that counts, but how well.

Too often the older person lives in the past instead of in the here and now. Old age, as well as all other periods of life, has its own usefulness and value. Old age should not be used as an excuse to cover up inability or unwillingness to adapt to new situations. Pity for the old is a poor substitute for the love and approval that are earned as the result of continued contribution to the family and the community. "Pity leads to overprotection and then to rejection."

Although there is a great need for more and better facilities to care for the aged who are ill or who have no place to live, there is a greater need to develop the human relationships of older people. "More important than a home of one's own is a life of one's own." Dr. Lawton rejects the "grow old gracefully" motto, preferring "grow old aggressively, creatively, social-mindedly." Old age can be interesting and rewarding even if it is not glamorous. Financial security and good health, while important, are not as essential to a happy old age as usefulness. A wide range of interests, a willingness to learn and accept change, an active part in the life of the community—these are the means of achieving a good life to the end.

Dr. Lawton calls attention to a little stressed factor in the general attitude towards old age: "Whenever we try to evaluate the opportunities of the second half of life, we must recognize our own prejudice and hostility toward old people and our fear of growing old."

Ten pointers are given on "aging successfully" (which, incidentally, is the title of Dr. Lawton's forthcoming book). These include: (1) Admit that you are growing older. (2) Remember that aging brings "plus" changes as well as minus ones. (3) Answer "Too old!" with "Too old for what?"

New York

A recently published outline of state and local social welfare services in New York State shows that assistance to the aged is considered an important responsibility there. The Department of Social Welfare supervises 200 public and private homes for the aged and 554 hospitals and dispensaries, which care for the aged as well as the other population groups. Old age assistance is offered to needy persons, 65 or over, who are not living in a public home. During 1945 a monthly average of 104,361 persons received old age assistance, to a total of $47,186,994.

New York is at present revising its public welfare structure to prevent overlapping of services by local welfare agencies and to improve the efficiency of the system. Under the old setup, a wide variety of local agencies administered one or all of the eleven welfare programs. Under the new setup, there will be one convenient welfare office in each community where residents of the community may apply for any of the types of assistance offered, and a single staff will make all investigation on each application.

The Aged in Literature

The aged and the aging have always had a place in literature, says Helen Cintilda Rogers in the July-August number of *Special Libraries*, the official journal of the Special Libraries Association. Folk-lore, early Christian and Oriental religious writings, philosophy, poetry and fiction have all contributed to the volume of literature on old people. "We find through the ages not only a veneration for the aged, a responsibility for their care, and a protective attitude toward them as weaker members of society, but a respect for the wisdom of the old, and a reliance on their decisions and guidance in affairs of nations, communities, and families."

Sometime around the Victorian era, standard character types came into being. An elderly woman was depicted calmly knitting, giving advice on the home and children, and smiling sweetly. Old men told stories, gave sweetmeats to children, and carried an umbrella. Old people were not individuals, but all of a type; "they were gentle, sedentary, rich in the lore of the past, and inactive in contemporary affairs."

The machine age changed the status of the elderly. Old family values lost their importance, and the sense of family responsibility declined. Experience and judgment were no longer considered as highly in industry and business, and the man in his fifties or sixties was discharged. "The old were caught in the grinding wheels of progress and became a burden in our social and economic system, unable to adjust or be adjusted in the rapid change."

In literature, the old man and woman either continued in their former typed and unreal roles, or were depicted as useless in all the less pleasant aspects associated with aging.

In the twenties, the psychologist E. L. Thorndike startled attention by publishing the results of tests proving that, contrary to the popular belief that 'you can't teach an old dog new tricks,' the minds of older people are not rigid and incapable of learning. "Many of the older persons actually excelled younger ones in speed of learning because they were able from their experience to organize and analyze their subject and to pick out pertinent related data." The depression came along then, however, and Thorndike's findings were not put into practice in industry and business.

It was Walter B. Pitkin's *Life Begins at Forty* (McGraw-Hill, 1932) that sounded the trumpet call to widespread interest in the aged. A tremendous number of books and articles dealing with the problems of aging have followed. Many and varied organizations of and for old people were formed. Pensions and assistance for those who could no longer support themselves were put into law.

Medicine and social work have contributed most to the currently increasing volume of writings having to do with age. Fiction and drama, too, now frequently have older people as central characters or as strong supporting characters. Among the excellent books on aging are George Lawton's *New Goals for Old Age* (Columbia University Press, 1943), Lillian Martin and Clare de Gruchy's *Salvaging Old Age* (Macmillan, 1930) and *Sweeping the Cobwebs* (Macmillan, 1933), and M. W. Thewlis' *Care of the Aged*, now in its fifth edition (Mosby, 1946).

Turning from the aged in literature, to literature for the aged, Miss Rogers emphasizes the change in selecting reading material for grandfather and grandmother that has taken place in recent years. Instead of being confined to the Bible, religious and philosophical writings, poetry, and a little biography or historical fiction, older people today are interested in everything. They want to catch up on all they didn't have time to read when they were occupied almost exclusively with making a living. They want to read about the world in which they live today and the people in it. "Particularly are the aging interested in books that will help them adapt to a graceful, active, and likeable old age. They want to know the problems they face and how to avoid or meet them. They want to know about diets and physical and mental

hygiene. They want to know about hobbies and recreational activities, their own capabilities and limitations, and their place in the world of today."

Retirement

To defeat the dictionary definition of retirement it is well to start young, says Ray Giles in the August issue of *Better Homes and Gardens*. According to Funk and Wagnalls, to retire is "(1) to withdraw from circulation; remove from active service; (2) to go into privacy or seclusion; withdraw from public life; draw back." This would indeed be a dismal outlook for the ten or fifteen or twenty years that lie ahead of many persons when they retire. Fortunately it is entirely unnecessary.

Public service is a challenging outlet for energies no longer devoted to job or profession, and everyone need not run for mayor or alderman. There is need for workers in the primary elections. Perhaps the public library needs help with a money-raising drive. Interracial and interreligious understanding has a long way to go, and there are many organizations devoted to this purpose. Are there enough good playgrounds, or does public enthusiasm need to be aroused to promote them? Taking up a worthwhile cause is tremendously effective in restoring petty annoyances and personal discomforts to their true proportions.

There is an old saying, "Two occupations are better than one," which is especially true when one is an occupation that can be taken into retirement. Making such things as pipes for gifts and for sale; raising dogs; collecting rare stamps, coins, and other items in which people all over the world are interested and which can lead to interesting pen-friendships—these are a few of the many possibilities. Gardening, too, can be an interest-consuming pastime, but if it is to be of real and continuing satisfaction it would be well to have a goal in view for the garden—such as flowers or vegetables for a hospital or orphanage. In other words, hobbies with a purpose are better than hobbies just for fun.

Of course it is entirely possible for a man or woman to discover and develop late in life an unexpected talent—for painting, or writing, or music, or what not. It is never too late to learn. However, "preparing for the real satisfaction in your retirement is like caring for your hair and your teeth—you can't begin too early. So why not, today, begin planning and working—not for 'retirement' but for your second coming-out party?"

Social Security

Beginning on October 1 certain amendments to the Social Security Act went into effect, increasing by approximately $123,000,000 the annual amount of federal funds that can be granted to the states for old age assistance programs. The amendments are to be effective, however, for only fifteen months.

The maximum old age assistance payment in which the federal government is now allowed to share has been increased from $40 to $45 per month, and instead of matching state expenditures on a 50-50 basis as before, the federal government may now pay two thirds of the first $15 of the average monthly payment and one half of the remaining payments (up to the new maximum of $45). The government is also now sharing more of the administrative expense.

It is assumed that the states will add more persons to their benefit rolls and increase the amount of payments to present recipients, when the necessary changes in present state assistance laws are made, rather than use the additional federal money to supplant state and local funds.

Old Age in Canada

"The spotlight is on old age," says Amy B. Edwards, writing in the July 15 issue of *Canadian Welfare*. No civilization has ever

before had so many old people, and we are at last becoming aware that the relation of the aged to the community leaves much to be desired. Although in the past little has been done in the way of dealing with the individual needs of older people on a case work basis, the same basic principles apply to this age group as to all others. To live a satisfying life, old people as well as young need security, affection, and most important of all—a part in the life around them.

The first essential is some measure of financial security. In Canada, the maximum old age pension is $25 per month, so that old people who have no other source of income or support must inevitably adopt lower living standards and withdraw from almost all community activities. However even this small pension has brought some degree of security and independence.

Second in importance to financial security in a program for later maturity is medical attention. "Among the aged, the fear of illness, as well as the reality of it, is a constant threat to security in its wider sense." Up till now, emphasis in medicine has been on acute illness rather than chronic disease.

Next to health, in a recent survey made in Vancouver, old people were found to be more anxious to talk about housing than any other problem. They are always at a disadvantage in finding a place to live: Their funds are limited; they must be close to shops, churches, movies; they cannot walk up flights of stairs.

No one housing plan will solve the problem, for the needs and desires of the aged are as varied as those of any other group. However, privacy is a must, and the segregation of old people should be avoided. "The aged suffer from a sense of separation, and the more they can form part of a general community, the happier they will be."

Usually the hardest adjustment for an old person to make is to the role of a dependent person "whose opinions and advice are no longer of interest to the people around him." The compensations of old age have not been sufficiently stressed, nor have social and recreational opportunities been made available which can supplant the satisfactions of earlier life. The Second Mile Club in Toronto is a small neighborhood social center where old people may meet others of their own age and become again a part of a group. The Gordon House Community Centre in downtown Vancouver offers a wide program of activities to the large group of old folk who live in rooming houses in the locality.

With retirement being forced automatically upon many workers as they reach the age of 60 or 65, part-time and light employment could be made available through centers established for the purpose. Such centers could also offer occupational therapy and training for leisure time activities, combined with counselling and opportunities for social contacts.

In order to get such programs under way, some sort of committee on the aged might be set up under local welfare councils, but eventually the program should be broken down into neighborhoods.

"Science has greatly lengthened the span of life. Having brought a large section of our population to this greater age, there is now a further obligation upon society to see that they have a full share of opportunity to exercise their powers, both in conducting their own affairs and in contributing to the general life of the community."

A Common Attitude

A letter to the editor of *Hygeia* (June, 1946) expresses what is probably a common attitude towards the prolongation of life. After asserting that he had taken a "poll of the local citizenry," the correspondent declares that medical science is "dragging a bunch of oldsters past their prime. . . . They don't thank you for it but have only that much longer to grunt and groan. Why doesn't the medical profession quit patting itself on the back and recognize that it is only impeding a new generation by patching up its precursors?"

This attitude is based on two misconceptions. The first concerns how and why

it is that "a bunch of oldsters" are here today instead of only a few, as formerly. The second misconception has to do with the necessity of grunting and groaning throughout old age.

In past centuries, there were few old people because many people died in infancy or during childhood or during their active adult years—died instead of living to enjoy those periods of life which, by inference, *Hygeia*'s correspondent believes to be the only enjoyable periods. Naturally, fewer people having achieved maturity, fewer people lived to be old. In other words, many elderly people is merely the result of healthier younger generations.

The second misconception concerns the future welfare and happiness of these increased numbers of old people. Too often old age is considered only as a prelude to death—not as as important a stage of life as childhood, adolescence, and vigorous maturity. It is not too much to hope that before long many of the degenerative diseases which now cause so much suffering and concern to the older age group, such as heart disease, arteriosclerosis, and cancer, will be as controlled as many diseases of earlier life now are. Social security programs are laying a foundation of financial security for old age. Thus, reasonable health and moderate security for the aged are within sight.

Given those basic essentials, happiness in old age will be largely up to the individual. No period of life is free from its disagreeable features. Childhood is a maze of restrictions. Adolescence is beset with emotional insecurity. Maturity has always its ambition, tension, and strain, with never enough time to relax. Why should old age be feared because it, too, has its own peculiar problems to be faced?

Grandmothers

Grandparents are usually only honorary members of the family group, as long as the family remains intact. However, "grandparents, and especially the grandmother, reassume a sociological function the moment a gap has to be filled and missing members of the intermediate generation have to be replaced," says Hans Von Hentig in the May issue of *Social Forces*.

The war created many such gaps. Fathers were taken into the service, and mothers went to work, often leaving the children in the care of the grandmother. In the wake of the war came an increase in divorce, desertion, and illegitimacy; the housing shortage; and the unemployment phase of reconstruction. In many cases it is the grandmother who takes in the grandchildren, and receives children and grandchildren in her home when the family cannot find living quarters or the father cannot find work. "The lower mobility of the older generation renders her more shockproof to the contingencies and fortunes of industrial life."

There are roughly about eleven million active grandmothers in the United States. This figure includes also the childless "grandmothers"—women between the ages of 45 and 69 who did not bear children. These women sometimes take care of grandnieces and nephews. Many more grandmothers live in rural areas than in cities, and this fact adds to their stability and value in the postwar crisis.

"The grandmother enjoys special prestige among the colored people." Colored races have generally a more matriarchal society, and superstition shrouds the grandmother with unusual power to ward off bad luck. Grandparents among the American Indians likewise had an important role, being the depositaries of knowledge and wisdom. Old age was usually a happy time for Indians, for they were held in respectful awe.

In contrast, the grandmother of the white race assumes a vital role in the life of the family, for the most part only when emergencies, such as death, divorce, desertion, and migration, tear the family apart.

LEGAL ASPECTS

The following are extracts from the bulletins on state legislation, health and welfare, of the Social Security Board. Errors may occur in both bill numbers and titles.

CALIFORNIA

Aged, Care of—S.32X. Amends Section 2302 of the Welfare and Institutions Code, relating to the inspection services for licensing agencies for the care of the aged; makes an appropriation therefore; declares the urgency thereof, to take effect immediately. Approved March 5, 1946. Chapter no. 107.

LOUISIANA

Old Age Pensions—H. 59. Provides for old age pensions by using the excess in State Bond and Interest Tax Fund; authorizes issuance of bonds. Introduced May 14, 1946; referred to Judiciary Committee.

Aged and Blind, Assistance—H. 166. Repeals Section 18, Act no. 359, 1938 Laws, as amended, relative to the recovery from the estate of a recipient of old-age assistance or aid to the needy blind. Introduced May 20, 1946. Amended and passed in Senate June 28. Approved July 11, 1946. Chapter no. 62.

MASSACHUSETTS

Old Age Assistance, Aliens—H. 293. Extends the benefits of the old age assistance law to certain persons not citizens of the United States. Introduced Jan. 7, 1946. Referred May 13 to 1947 annual session.

Old Age Assistance, Eligibility—S. 41. Reduces the age at which persons shall be eligible to receive old age assistance to 60 years. Introduced Jan. 2, 1946. Reported unfavorably in Senate May 6. Killed in Senate May 7.

Food Allowances—H. 1892. Provides for increasing the food allowances in the state standard budget for the administration of old age assistance in municipalities. Introduced May 8, 1946. Killed in Senate May 23.

Old Age Assistance—H. 394. Equalizes the minimum monthly payments under the old age assistance law. Introduced Jan. 9, 1946. Killed in Senate May 23.

Old Age Assistance, Insurance Policies—H. 1643. Relates to insurance policies held by an applicant for old age assistance. Introduced March 26, 1946. Passed House May 23. Passed Senate May 29. Approved June 6. Chapter no. 460.

Old Age Assistance, Medical Care—S. 259. Relates to the furnishing of medical care to recipients of old age assistance. Introduced Jan. 14, 1946. Recalled from Governor and killed in Senate June 4.

Old Age Assistance, Payments—H. 1169. Establishes minimum amounts to be paid under the old age assistance law. Introduced Jan. 17, 1946. Killed in Senate May 23.

Old Age Assistance, Budgets—S. 160. Increases the food and clothing budget in the old age assistance law. Introduced Jan. 10, 1946. Taken from table in Senate June 12 and referred to 1947 annual session.

MISSOURI

Old Age Assistance, Eligibility—S. 23. Establishes the 1944 valuation as a basis for evaluating the dwelling houses of needy persons as it applies to the determination of eligibility for old age assistance. Introduced Jan. 30, 1945. Went to conference in Senate June 26. Conference report rejected in Senate June 26.

PNEUMONIA IN THE AGED

Pneumonia in the aged has been set apart from the disease in younger individuals by the terms senile, terminal, and hypostatic pneumonia. These terms suggest that the disease is a part of old age rather than an active infection. They imply an unjustified hopelessness and induce a feeling of defeatism in the physician.

Osler (The Principles and Practice of Medicine, D. Appleton-Century Company, New York, 1944, fifteenth edition) regarded pneumonia as the friend of the aged. "Taken off by it in an acute, short, not often painful illness, the old escape those 'cold gradations of decay' that make the last stage of all so distressing."

Heffron (Pneumonia with Special Reference to Pneumococcus Lobar Pneumonia, Commonwealth Fund, New York, 1939) has reported the incidence as high as 2,000 per 100,000 in persons over 70, compared with an incidence of 640 in the age group 15 to 20 years. Factors which influence the occurrence and modification of pneumonia in the aged are the general and local changes associated with senescence as well as the high incidence of associated diseases. Immunologic changes have been emphasized by Kaufman (Archives of Internal Medicine, *67:* 304–319, 1941), who attempted to raise the bacterial antibody titer by the use of antigenic pneumococcus polysaccharides in old age.

Zeman and Wallach (Archives of Internal Medicine, *77:* 678–699, 1946) studied 166 cases of pneumonia in men and women 60 years of age and older. In this series there was a mortality of 33, or 20 per cent of the total. The mortality rate of 23 per cent in men and 15 per cent in women suggested an increased resistance to pneumonia in older women. Sixty-five cases were attributable to pneumococci, with 8 deaths, a mortality rate of 12 per cent. Pneumococcus Type III was most common, but Type XX was most virulent. Streptococcus pyogenes accounted for 6 cases. Twelve cases of primary atypical or virus pneumonia occurred, none of which was fatal. Of the 7 cases of suppurative bronchopneumonia, 5 terminated fatally. Cases of pneumonia of undetermined origin numbered 73, with a mortality rate of 24.6 per cent.

Among the conditions Zeman and Wallach found most frequently associated with pneumonia in the aged were cardiovascular, pulmonary, nutritional, and cerebral diseases. Preexisting pulmonary disease is attended with far lower mortality than associated cardiovascular disease or diabetes. In addition to the influence of coexisting diseases, the diagnosis of pneumonia in an old person may be obscured by unusual modes of onset and by an atypical clinical course. The pneumonic infection may be completely latent clinically. It may be dominated by toxic mental symptoms. Uncommonly the pneumonia may have a completely afebrile course. Relapsing and recurrent forms are encountered in which the illness may spread over the course of several months.

To establish the diagnosis of pneumonia in the aged, Zeman and Wallach regard a

careful history and physical examination essential, but the symptoms may be masked, confusing, or difficult to elicit. Sputum and blood cultures may be helpful, but the most valuable aid is the x-ray. The principle complications other than those connected with the associated diseases are empyema, meningitis, and endocarditis. Empyema is less common since the advent of chemotherapy. Pneumococcic meningitis can be successfully treated with penicillin and sulfonamide drugs. Pneumococcic endocarditis was present in the aged in 3 cases reported on by Zeman and Siegal (American Heart Journal, *29:* 597–610, 1945).

The prognosis in pneumonia depends upon many factors, such as the multiplicity and severity of the associated diseases. The type of organism and the number of lobes involved also play important roles. The prompt recognition of the existence of a pneumonia and the early use of chemotherapy with appropriate supportive measures constitute the essential factors in treatment of pneumonia in the aged. The patient should be made comfortable in bed and encouraged to change his position and move his legs. The blood count and urine must be checked frequently if sulfonamides are administered. The use of oxygen inhalation may be of inestimable value.

Although the mortality rate has been dramatically reduced by recent advances in therapy, pneumonia is still a disease with high incidence and high mortality in the aged. The therapeutic results in the presence of complications indicate that the associated lesions may be treated successfully along with the pneumonia. Active treatment of the pulmonary infection and associated conditions must be undertaken no matter how overwhelming the odds seem to be against recovery.

FRANK VELLIOS

CLIMACTERIC—MALE AND FEMALE

General interest in this highly controversial subject is and probably has always been as widespread as the human race itself. This is particularly true of the sexual functions of the aging man, partly because of the traditional acceptance of the inevitability and immutability of the female climacteric, with its obvious menopause, and partly because of the almost universally patriarchal or male-dominated civilizations, in which virility and fertility have been highly regarded. Thus, the number of witch-doctors, high priests, medical practitioners, charlatans, and visionaries, from antediluvian times through the twentieth century, who have specialized in turning back Time in its flight, is incalculable.

An empiric appreciation of sexual atrophy is at least as old as early Biblical times (Genesis 17: 15–17), but it was not until 1849 that the scientific approach to the problem of declining sexual function was heralded by Berthold (Archiv für Anatomie, Physiologie, und wissenschaftliche Medicin, *16:* 42–46, 1849), when he recorded the successful prevention of signs of castration in capons into which he had transplanted gonads. Attempts to isolate an active testicular principle to stave off old age were frequent, and in 1889 Brown-Séquard, at the age of 71, wrote with enthusiasm of the effects on himself of injected extracts from the testes of guinea pigs and dogs (Comptes rendus des séances de la Société de biologie, *1:* 420, 1889).

A review of the physiologic changes in the climacteric is given by McCullagh (Cleveland Clinic Quarterly, *13:* 166–176, 1946), with a critical evaluation of diagnostic criteria, based on experimental data of his own experience. There is little disagreement in the literature on the functional changes incident to the female climacteric, although few writers take the teleologic view of the process advanced by

Owen (American Journal of Psychology, *101:* 756, 1945). McCullagh discusses the female climacteric as a normal process, involving primarily the ovary, and of which the menopause is usually an incident but by no means always, as menopause may precede or succeed other symptoms of ovarian failure. According to his description, the ovary in advancing age gradually and increasingly fails to respond to the stimulation of the gonadotrophins of the anterior pituitary, as a result of which there is no ovulation, no corpus luteum, and no progesterone. Eventually the follicular hormones fall to such a low level that the endometrium no longer responds, and menstruation is at an end. Associated changes include atrophy of the various secondary sexual organs, all dependent on lowered levels of blood estrogen, and at least partially reversible by substitution therapy.

A striking hormonal change in the climacteric is an elevation of the gonadotrophin excretion in the urine, associated with an increase in basophilic elements of the anterior pituitary. This phenonenon is attested to frequently throughout the literature, both in connection with the climacteric and in the functional or anatomical castrate; the high titer of gonadotrophins apparently continues indefinitely, unless depressed by estrogenic replacement therapy (Best and Taylor: The Physiological Basis of Medical Practice, Williams & Wilkins, Baltimore, 1943, third edition, ch. 62; Goodman and Gilman: Pharmacological Basis of Therapeutics, Macmillan, New York, 1941, ch. 67; Albright: Endocrinology, *20:* 24, 1936; Owen: American Journal of Psychology, *101:* 756, 1945).

The mechanism of symptoms of the female climacteric are not so easily correlated. McCullagh cites evidence against the suggested causal factors of elevated levels of gonadotrophin and adrenal androgens. He quotes Hawkinson (Journal of the American Medical Association, *111:* 390, 1938) and others to indicate the high incidence of distressing menopausal symptoms among women, reaching 75 to 85 per cent, although only 10 per cent of these were incapacitated. A list of symptoms is given by McCullagh and discussed briefly, with emphasis on careful evaluation of the individual patient to eliminate unsuspected organic disease, such as hypertension, thyroid disease, or carcinoma. Diagnosis of the female climacteric is said not to be difficult in most cases, though amenorrhea in the younger groups may suggest pregnancy; in these cases the elevated gonadotrophins of the climacteric may cause false positive biologic tests for pregnancy. Many symptoms respond promptly to substitution therapy with estrogens, while others are refractory. Menopausal arthralgia, vasomotor symptoms, mild mental depression, pruritus, and senile vaginitis are easily correctible, while involutional psychoses, weight gain, and various psychosexual behavior tendencies, such as frigidity, probably require supplementary therapy. The treatment of menopausal symptoms is described as both medicinal and psychiatric. The natural or synthetic estrogens control the more disturbing symptoms, given in connection with reassurance and understanding, and suggestions for adjustment to the new life status.

In striking contrast to the frequency of the female climacteric, the so-called "male climacteric" is described as a distinct rarity by McCullagh, so that the word, climacteric, is a misnomer, in that it implies a normal physiologic functional change at a certain age in most men. The medical literature abounds with articles on this subject, and in general the authors can be grouped in three categories: (1) those who believe the male climacteric to be a definite clinical entity, not uncommon, fully deserving the title of climacteric, and who consider the subjective symptoms most important and dependable for the diagnosis (McGavach: Journal of Clinical Endocrinology, *3:* 71, 1943; Owen: American Journal of Psychology, *101:* 756, 1945; and Werner: Journal of the American Medical Association, *127:* 705, 1945); (2) those who

hold that the male climacteric is an uncommon occurrence, but deserves thorough study to eliminate pure psychogenic complaints (McCullagh: Cleveland Clinic Quarterly, *13:* 166, 1946; Heller and Nelson: Journal of Clinical Endocrinology, *5:* 1–33, 1945; Cowdry: Problems of Ageing, Williams & Wilkins, Baltimore, 1942, second edition, p. 491); (3) those who claim that primary testicular insufficiency is rare indeed, and that the diagnosis should be lifted from the clinical level of subjective symptoms as much as possible to the laboratory level of hormonal assays and other objective studies (Hamilton, Catchpole, and Hawke: Journal of Clinical Endocrinology, *5:* 204, 1945).

McCullagh outlines the subjective and objective findings in male postpuberal castrates, and in general they are similar to those of the climacteric woman. Heller and Nelson (Journal of Clinical Endocrinology, *5:* 1–33, 1945) describe in detail the findings, both subjective and objective, in their series of cases of testicular insufficiency to support their diagnosis of the male climacteric, and cite the favorable results of androgenic substitution. Abarbanel, on the contrary (Journal of the American Medical Association, *127:* 419, 1945), denies the specificity of testosterone therapy, doubts that testicular failure is solely responsible for the climacteric, and finally, claims that the "climacteric stems from a disturbance of the heat regulatory mechanisms from a lowering of certain steroids." In short, facts are difficult to ascertain, and the controversy in the literature is not yet at an end.

In general, there is agreement on the basic changes in testicular insufficiency, whether from castration or from unknown cause. McCullagh summarizes these changes briefly in his series of 60 cases of unstated age. The symptoms included nervousness, lassitude, decreased libido and potentia, and in one-quarter of the group, hot flashes. Heller and Meyers (Journal of the American Medical Association, *126:* 472, 1944) and Hamilton, Catchpole, and Hawke (Journal of Clinical Endocrinology, *5:* 204, 1945) describe a total of 31 unselected men between the fifth and tenth decades of life, none of whom showed any significant deviation in gonadotrophin titer from that of young, normal men. In general, the gonadotrophin titer is taken by most investigators as an indicator of testicular function. Androgen excretion, in 6 cases of McCullagh's series, was normal in 2 and low or borderline in 4. Assays of 17-ketosteroids in 33 cases were low or borderline in 30. Gonadotrophin assays showed between 53 and 67 per cent of the cases to have elevated values. These figures are generally less spectacular than those of Heller and Myers, who found 23 of 38 cases with climacteric symptoms to have markedly increased gonadotrophin excretion. The remaining 15 cases were classified as psychoneurotic and psychogenically impotent on the basis of the tests mentioned previously and the fact that none responded to a therapeutic test of testosterone. All of a representative number from the 23 cases exhibiting evidence of testicular insufficiency were found to have histologic confirmation of the clinical diagnosis. McCullagh, on the contrary, found that only 16 per cent of his series improved on testosterone therapy (of unstated dosage, "known to improve the symptoms which follow castration").

McCullagh closes his article with the suggestion that there is need for critical evaluation of the subject of testicular insufficiency before general use of the term male climacteric can be approved.

JAMES G. OWEN

ELECTRIC SHOCK THERAPY

The electric method of inducing convulsive seizures of the grand mal type for the treatment of mental disorders was introduced in 1937 by Cerletti and Bini. In

early descriptions of the technique and the advantages of the method, the belief was expressed that the contractions were less violent and trauma less severe with electric than with drug stimulation (Shapley and McGregor, British Medical Journal, *2:* 1269–1271, 1939). Clinical investigation has shown that the incidence of fractures shows no appreciable variation with either method (Kraines: The Therapy of the Neuroses and Psychoses, Lea and Febiger, Philadelphia, 1943, p. 454). Curarization has greatly reduced the number of traumatic complications (Cash and Hoekstra: Psychiatric Quarterly, *17:* 20–34, 1943) and the hazard to patients with osteoporosis.

In an appraisal of convulsive shock therapy in elderly patients by Evans (American Journal of Psychiatry, *99:* 531–533, 1943), who used metrazol or electric shock in his series of 50 patients, it is pointed out that severe cardiovascular disease is a contraindication to either method. Palmer, in an article published posthumously (Geriatrics, *1:* 60–79, 1946), states that there is specific indication for electroshock treatment of the patient over 65 in the severe depressions of involutional melancholia and of the manic-depressive psychoses. He further states that complications are few and gives a recovery rate of 85 to 90 per cent in an unspecified number of cases of involutional melancholia treated with electric shock and curare.

A more critical evaluation of this method applied to patients over 65 years of age has been made by Feldman, Susselman, Lipetz, and Barrera at Albany Hospital, New York, in the *Archives of Neurology and Psychiatry* (*56:* 158–170, 1946). In this investigation 53 patients between the ages of 65 and 82 years were treated with varying numbers of electrically induced convulsions for several mental disorders. In addition, the literature pertinent to the method and age group is reviewed, and complications and contraindications are discussed. The study covered a three and a half year period from 1941 to 1944.

Analysis of the case material in the series of Feldman, Susselman, Lipetz, and Barrera is made with reference to psychiatric diagnosis and physical status. Diseases treated were: "depression"—36 subjects, of whom the majority were suffering from involutional melancholia; manic psychosis—4; psychoneurosis with depression—7; and paranoid psychosis—6. Recovery was reported in 11 subjects suffering from depression and 1 with psychoneurosis. All groups showed varying degrees of improvement, while the least favorable response was obtained in the manic state and paranoid psychosis. Certain criteria are cited to determine the degree of cardiovascular impairment, and 20 patients were found clinically to have little or no sign of heart disease. Among the 33 who showed deviations from the prescribed normal clinical standards there were variations of considerable degree. In only one case was it necessary to discontinue treatment because of regression of the cardiovascular status. Other manifestations of disease were present but showed no aggravation by treatment.

The importance of differentiating between psychotic depression and dementia is emphasized in this study. The latter condition is either aggravated or not improved by electric shock therapy. In 3 patients, deterioration was so rapid and obvious under treatment that the method was discontinued after two to six shocks. When the differentiation is unusually difficult, or senile dementia and depression are believed to coexist, several shock treatments may be used as a therapeutic test or method of determining the quantitative effect of each disease.

Hospital care and complications are discussed, the complications putting additional emphasis on the need for thorough and repeated examination of the cardiovascular status of the older patient both before and during treatment. No fatalities occurred in this series.

The study of Feldman, Susselman, Lipetz, and Barrera concludes with a review of the literature and an analysis of

the causes of death in the 19 patients reported in the literature as succumbing to electric shock treatment, regardless of age. The investigators add one case of their own (under 65 years of age) and discard 3 as being fatalities irrelevant to the shock therapy. Documentation, clinical, and necropsy data are inadequate in many of these fatal cases. Of the 17 fatalities discussed, 3 patients were over 65 years of age. These three were considered "greatly increased risks" prior to the institution of convulsive shock treatment, and death was believed to be of cardiac origin. Six younger subjects not previously considered as presenting any contraindications to treatment were listed among the fatalities.

From this study it is concluded that electric shock treatment can be of great value in elderly patients, provided that a correct psychiatric diagnosis is made and the disease has been shown amenable to such treatment, and that cardiovascular impairment is not severe. When there is doubt concerning the physical status, fine judgment is required to determine whether or not the possible benefits of therapy outweigh the risks involved.

OSCAR N. RAMBO, JR.

HEPATIC FUNCTION IN PSYCHOSES

During the last thirteen years a nunber of articles have appeared in the literature regarding the impairment of liver function, as reflected by a lowered excretion of hippuric acid in the urine after administration of sodium benzoate, in patients with psychoses. A recent report by Stern, Hinds, and Askonas (American Journal of Psychiatry, *102:* 325–329, 1945) deals more specifically with the results of intravenous hippuric acid tests in patients with psychoses, the majority of whom (47 of 71 patients) were 45 years of age or older.

Examples of diseases in which the liver and brain show related changes are Wilson's disease, and kernicterus observed in erythroblastosis foetalis. Since Quick (American Journal of the Medical Sciences, *185:* 630–635, 1933) presented the hippuric acid test as a feasible test for impairment of liver function, several authors have correlated results of this test with the presence of psychotic conditions, especially the catatonic state of schizophrenia. Quastel and Wales (Lancet, *238:* 402, 1940) and Davies and Hughes (Lancet, *238:* 403–405, 1940) corroborate the original work of Quastel and Wales (Lancet, *235:* 301–305, 1938) as referred to by Stern, Hinds, and Askonas, that a majority of patients with catatonic schizophrenia show a decreased urinary hippuric acid excretion after administration of sodium benzoate, and that a small group of patients with other types of schizophrenia show some impairment of hippuric acid excretion. On the other hand, Ström-Olsen, Greville, and Lennon (Lancet, *235:* 995–996, 1938) and Finkelman, Hora, Sherman, and Horwitt (American Journal of Psychiatry, *96:* 951–960, 1940) found that less than one fourth and less than one half, respectively, of their patients with catatonic schizophrenia showed lowered hippuric acid excretion.

In the investigation by Stern, Hinds, and Askonas, 71 patients with psychoses were examined for evidence of impairment of liver function by the intravenous hippuric acid excretion test of Quick. Forty-seven of these patients were 45 years or older and suffered from disorders, organic or affective, that arose during the involutional or old age period. None of the patients showed evidence of liver disease or gross metabolic disorders by clinical or laboratory examination, including fasting blood sugar and cholesterol levels. Patients with arterial hypertension or slight to moderate elevations of the nonprotein nitrogen level showed no changes in hippuric acid excretion that could be correlated with either the hypertension or the

increased NPN. Changes in hippuric acid excretion could not be correlated with either body weight or source of diet (some patients were in institutions, others were not).

In 24 of the 30 patients over 60 years of age in the group, 80 per cent showed definite impairment of ability to excrete benzoic acid as hippuric acid. Rafesky and Newman (American Journal of Digestive Diseases, *10:* 66–69, 1943), as referred to by Stern, Hinds, and Askonas, report that of patients 60 years or older without physical or mental impairment, only 24 per cent showed lowered ability to form and excrete hippuric acid. Five patients with senile dementia showed the greatest impairment in liver function, according to the test used.

A larger series of similar tests obtained by collecting other small series as they appear in the literature may be helpful in drawing definite conclusions about the material presented by Stern, Hinds, and Askonas, who, themselves, refrain from any definite interpretation of their findings. This would seem wise in view of the somewhat contradictory results previously mentioned concerning hippuric acid excretion in patients with catatonic schizophrenia. It has been suggested (Lichtman: Diseases of the Liver, Lea & Febiger, Philadelphia, 1942, pp. 330–331) that the formation of hippuric acid from sodium benzoate and glycine in the organism be called conjugation rather than detoxification, thus substituting a descriptive for a teleological term.

BETTY BEN GEREN

CARE OF THE CHRONIC AGED SICK

Marjory W. Warren, M. R. C. S. and Deputy Medical Director of the West Middlesex County Hospital, Isleworth, outlines a plan for the care of the chronic aged sick in Great Britain in the June 8, 1946 issue of *The Lancet.* The plan is one of many which are being offered, for, in Britain as in the United States, with the aging of the population the problem of caring for the aged sick is a huge and ever increasing one.

Dr. Warren's plan is devoted to the "over 60" age group, and is a medical plan, built to use the existing general hospitals. The key feature is the creation within the general hospitals of geriatric units, which would diagnose and determine the disposition of all those requiring care. Since these units would enjoy the same "full facilities and stimulating atmosphere" as the existing pediatric, orthopedic, psychiatric, and other units, they would do much to increase qualitatively and quantitatively the specialized medical care of the old age group. Nursing care, a great factor in treatment of elderly patients, would improve as the attitude and enthusiasm of attending physicians improved.

Dr. Warren divides the aged sick into two classes—those who can remain in their own homes, and those who cannot. The latter class, according to Dr. Warren's plan, would be divided into two groups: those who must remain in the geriatric hospital unit for treatment, and those who may be cared for in a nursing home.

Those who must remain in the hospital would have specialized nursing care as required, and daily attendance of a medical officer and "regular full medical rounds." Those placed in nursing homes would have constant nursing supervision and care and a doctor "on call." The nursing homes would be attached to the hospital unit, thus enabling the patients in the homes to profit from the hospital work-up. Rehabilitation of patients would be emphasized, to be accomplished by the combined efforts of medical and nursing personnel, physiotherapists, occupational therapists, and social workers.

Dr. Warren deplores the prevalent treatment of and attitude toward the aged chronic sick and offers this plan to help correct the situation. There is a big market for such a plan, and Dr. Warren tries hard to sell it.

JOSEPH W. NOAH

TESTOSTERONE AND SEXUAL IMPOTENCY

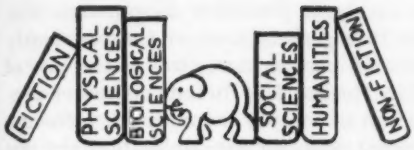
It is generally accepted that men experience a loss or some decrease of libido and potency with advancing age. Werner (Journal of the American Medical Association, *127:* 705–710, 1945) considered the subject of the male climacteric and reported his observations on 54 men averaging 50.5 years of age. He found a decrease or loss of potency in 90.8 per cent, and a decrease or absence of libido in 75 per cent. Other symptoms associated with the syndrome of the male climacteric were classified as nervous and circulatory, with subjective nervousness occurring in all of the patients studied. Werner found, as had Heller and Myers (Journal of the American Medical Association, *126:* 472–477, 1944), that the male climacteric syndrome was or could be the result of testicular hypofunction or afunction. Both advocate the use of testosterone in the treatment of the syndrome, but Werner warns: "Testosterone should not be given for the purpose of stimulating potency. While it occurs in some patients, this result cannot be promised and it is perhaps better for older men if this phase of the reaction does not result."

In relation to the clinical observations on the male climacteric, the recent report of Minnick, Warden, and Arieti on "The Effects of the Sex Hormones on the Copulatory Behaviour of Senile White Rats" (Science, *103:* 749–750, 1946) demonstrates that both testosterone and pituitary-like hormone will increase the copulatory activities of aged male white rats. In their experiment, three groups with 8 white rats in each were observed. One group received large doses of testosterone propionate; the second group received anteron (pituitary-like hormone from pregnant mare's serum); the third group served as controls. In the copulatory tests each rat was exposed individually for ten minutes to a female in heat. Exposures were made on the eighth and fifteenth days of the experiment. Only 3 animals of the control group exhibited copulatory behavior while the two experimental groups had a fairly high copulatory score, though 2 of the animals of each of these experimental groups did not copulate at all.

Minnick, Warden, and Arieti concluded that rather large doses of testosterone propionate were no more effective than pituitary-like hormone in stimulating the copulatory activity of senile rats. They assumed that the pituitary-like hormone operated as an activator on the interstitial cells of the testes. This view was supported by the histologic findings of hypertrophy and hyperplasia of the interstitial cells of the testes of the group receiving pituitary-like hormone. The testes of the rats receiving testosterone showed some degree of atrophy of the interstitial cells with replacement fibrosis. On the basis of this finding, Minnick, Warden, and Arieti question the advisability of using testosterone propionate in replacement therapy.

This experiment raises a question regarding the clinical use of testosterone that should be considered carefully. The beneficial results obtained clinically in the treatment of the male climacteric with testosterone indicate the usefulness of the preparation. However the use of testosterone in the treatment of sexual impotency alone should not be undertaken indiscriminately if at all. Further observations of the effects of testosterone on the tissues of men and animals should be made to clarify the point raised by Minnick, Warden, and Arieti as to its harmful effect on the testicular tissues if given in large doses or over a long period of time.

FRANK M. TOWNSEND



BOOKS

PHYSICAL CHEMISTRY OF CELLS AND TISSUES, Rudolf Höber, with the collaboration of David I. Hitchcock, J. B. Bateman, David R. Goddard, and Wallace O. Fenn, The Blakiston Co., Philadelphia, 1945. $9.00.

This is an authoritative presentation of a field of investigation which has come to be called "general physiology"—that is, an attempt to explain the nature and function of cells and tissues on first principles. The most logical approach to biology and medicine would seem to be through a systematic study of the physics and chemistry of increasingly more complicated systems, starting with atoms and ending with sick human beings, or perhaps even with sick society. The successful pursuit of such a research program would logically approach —at some very distant time—an understanding of all nature and the simultaneous solution of many human problems. It has been, of course, unnecessary and unwise to postpone the more complicated problems until the simpler ones have been completely elucidated. Thus, insulin was discovered and put to humanitarian use more than twenty years ago, and yet it cannot be said that carbohydrate metabolism is even now completely understood, and the mechanism by which insulin affects this metabolism is only just beginning to be understood. However, for the solution of many other problems, the long sure road of the general physiologist must be traveled.

Höber and his collaborators have contributed a skillfully integrated monograph which might well serve as a textbook of general physiology. The objective, which seems to have been achieved to the extent that present knowledge permits, is to describe in physical chemical terms various chemical systems from the simplest atomic configurations to the highly complex aggregations of cells and tissues. It is an approach to physiology "from below."

An introductory section on those principles of physical chemistry which are particularly pertinent to cell physiology is contributed by Hitchcock, who has previously written a monograph on the subject. Bateman has written an excellent section on the properties and structure of large molecules and the forces between atoms and molecules. The content of this section derives in large part from quite recent studies of molecular configuration and of inter- and intramolecular forces. Following these two fundamental sections, Höber has presented several sections on the physical chemistry of actual living systems. Much of this material stems from Höber's own researches. These sections demonstrate how intensively have been studied the factors which affect the distribution of materials in cells, the ability of various substances to pass the cell wall, and the capacity of cells to actively absorb or excrete a variety of compounds. However, these chapters also reveal how very far science is from being able to explain more than a small fraction of the functions of living systems in exact physical terms. The book is completed by a section by Goddard on cellular oxidations and the enzymes which are responsible for these oxidations, and a section by Fenn on muscular contraction, to a knowledge of which he and his laboratory have contributed so richly.

It would seem to be of considerable convenience to biologic investigators, including students of the aging process, to have in a single volume the material that is presented, and the general point of view which

runs through the book—that cells and cell processes can ultimately be described in exact terms—should be of great value.

OLIVER H. LOWRY

THE PROLONGATION OF LIFE, Alexander A. Bogomolets, Duell, Sloan & Pearce, Inc., New York, 1946. $1.50.

This book is a translation from the popular Russian book which sold millions of copies in the U.S.S.R. It was published in the United States under the auspices of the Robinson Foundation. The general format of the book is good and the type clear and readable.

Professor Bogomolets' antireticular cytotoxic serum (ACS) is one of the most controversial subjects in the medical field today. The technical description of the preparation and use of ACS for the treatment of certain injuries appeared in the December, 1943 issue of *American Review of Soviet Medicine*. Popular interest in ACS was stimulated by the article by William Laurence in the December, 1945 *Ladies' Home Journal* and the abstract of this article in the March, 1946 *Reader's Digest*. Other accounts have appeared in the *American Weekly* and several popular books on medicine. Consequently the publication of the book is very timely and is of interest to the general reader as well as the trained investigator.

Antireticular cytotoxic serum in small doses is claimed to increase resistance to infection, to accelerate the knitting of bone fractures, and to stimulate the body via the reticulo-endothelial system; in larger doses cytotoxic action is claimed for cancer cells. These points have been verified in vitro by Drs. Pomerat and Anigstein of the Texas Medical College. In vivo, work is indecisive, according to Dr. Harry Goldblatt of Cedars of Lebanon Hospital. Some of the poor effects reported result from poor designing of the experiments. ACS works best on old animals and patients, and is ineffective or little effective in young animals, in which resistance to infection is highest.

In his book Professor Bogomolets discusses in a general manner the previously mentioned claims in regard to the use of ACS in Russia. His further claims of prolongation of life are emphasized, although this point was not especially brought out in the technical reports received from the U.S.S.R. He discusses the regeneration of cells in regard to long life and also several reported instances of longevity. Some of the examples are from newspaper accounts and consequently need to be verified further. The important European theories of old age are mentioned, especially Metchnikoff's theory of chronic poisoning of the cells by waste products.

Professor Bogomolets takes the commendable attitude that the prolongation of life is still a major problem and will probably not be solved by any one treatment, even ACS. In fact, he stresses the well known principles of moderation, with physical and mental activity important to longevity, as well as any discovered, or discoverable, aids to the lengthening of life.

The scientist will find that Bogomolets' book suffers from the lack of availability of American work on aging and, perforce, a greater reliance on European sources, which are somewhat behind recent American work in many respects. The general reader will find the book stimulating and suggestive for the development of work on aging as well as the general treatment of specific diseases suggested by Bogomolets. From the technical standpoint, the most serious weakness is that dosage in complementary titers and frequency of treatment are not included in the discussion. Such suggested data by Bogomolets, even if included as a footnote, would have enhanced the value of the book for investigators in the field of aging.

The student and investigator in the field of aging, the general reader, and members of the medical profession will enjoy this little book for its stimulating viewpoint, even if ACS does not prove to have all the advantages claimed for it. Sufficient of its

advantages have already been proven in this country to justify the production of ACS in the next year or so. The scientific investigator should not forget that ACS has been renamed in this country by some investigators to reticulo-endothelial immune serum (REIS).

The Robinson Foundation is to be congratulated on putting this book before the American public.

THOMAS S. GARDNER

BOOKS RECEIVED

Books received since July 1, 1946 are acknowledged in the following list. Insofar as space and time permit, some will be selected for review in a later issue, but it is unlikely that all will be reviewed.

The Prolongation of Life, by Alexander A. Bogomolets; Duell, Sloan & Pearce, Inc., New York, 1946, $1.50, 99 pages. (Reviewed in this issue, p. 488.)

Experimental Hypertension, New York Academy of Sciences, New York, 1946, $3.75, 179 pages.

Creative Old Age, by Clare de Gruchy, Old Age Counselling Center, San Francisco, 1946, $2.75, 160 pages.

The Best Years: How to Enjoy Retirement, by Walter B. Pitkin, Current Books, Inc., New York, $2.00, 194 pages.

United States Life Tables and Actuarial Tables for 1939–1941, United States Department of Commerce, Bureau of the Census, U. S. Government Printing Office, Washington, D. C., $1.25, 153 pages.

INDEX TO CURRENT PERIODICAL LITERATURE

It is difficult to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or send reprints. —Editor.

ANDREW, WARREN—Age Changes in the Vascular Architecture and Cell Content in the Spleens of 100 Wistar Institute Rats, Including Comparisons with Human Material. *American Journal of Anatomy, 79:* 1–73, 1946.

ARIETI, S.—(See Minnick, R. S., C. J. Warden, and S. Arieti.)

ARONSTAM, E. M.—Biliary Disease in the Elderly and Chronically Ill Patient. *New York State Journal of Medicine, 46:* 1117–1119, 1946.

ASKONAS, BRIGETTE A.—(See Stern, Karl, Ewart G. Hinds, and Brigette A. Askonas.)

BARRERA, S. EUGENE—(See Feldman, Capt. Fred, Lt. Samuel Susselman, Basile Lipetz, and S. Eugene Barrera.)

BILIARY DISEASE—Biliary Disease in the Elderly and Chronically Ill Patient. E. M. Aronstam. *New York State Journal of Medicine, 46:* 1117–1119, 1946.

BILLER, N. M.—New Patterns of Life for the Aged. *New York Times Magazine,* p. 23, June 2, 1946.

BOARDING CARE—Boarding Care for the Aged Sick. Sahra S. Rapp. *The Family, 27:* 192–196, 1946.

BOGOMOLETS—Bogomolets and the Longer Life. *Time, 47:* 92, 1946.

Can Science Double Your Life? J. D. Ratcliff. *Everybody's Digest,* July, 1946.

What Is the Natural Lifespan? M. Gumpert. *Saturday Review of Literature, 29:* 15, 1946.

CASSIRER, THOMAS—(See Stern, Karl, and Thomas Cassirer.)

CLIMACTERIC—Climacteric—Male and Female. E. Perry McCullagh. *Cleveland Clinic Quarterly, 13:* 166–176, 1946.

DE FORD, MARIAN A.—New Lives for the Old. *Everybody's Digest,* pp. 95–98, September, 1946.

DIEKE, S. H.—and C. P. Richter. Age and Species Variation in the Acute Toxicity of Alpha-Naphthyl Thiourea. *Proceedings of the Society for Experimental Biology and Medicine, 62:* 22–25, 1946.

EDWARDS, AMY B.—Adding Life to Their Years. *Canadian Welfare, 22:* 13–18, 1946.

FARRIS, SHIRLEY—and Harold E. Himwick. The Effect of Hypoglycemia and Age on the Glycogen Content of the Various Parts of the Feline Central Nervous System. *American Journal of Physiology, 146:* 389–393, 1946.

FELDMAN, CAPT. FRED—Lt. Samuel Susselman, Basile Lipetz, and S. Eugene Barrera. Electric Shock Therapy of Elderly Patients. *Archives of Neurology and Psychiatry, 56:* 158–170, 1946.

GENERAL—A Librarian's Working Knowledge of the Aged. Helen C. Rogers. *Special Libraries, 37:* 183–188, 1946.

Adding Life to Their Years. Amy B. Edwards. *Canadian Welfare, 22:* 13–18, 1946.

Care of the Chronic Aged Sick. Marjory W. Warren. *The Lancet, i:* 841–843, 1946.

New Lives for the Old. Marian Allen de Ford. *Everybody's Digest,* pp. 95–98, September, 1946.

New Patterns of Life for the Aged. N. M. Biller. *New York Times Magazine,* p. 23, June 2, 1946.

One Way to Live Longer. Laurence Lader. *Coronet, 20:* 36, 1946.

Research on Ageing. *The Lancet, ii:* 249–250, 1946.

So You Want to Live Long. George Lawton. *Ladies' Home Journal, 63:* 202, 1946.

GILES, R.—Why not Rehearse Your Retirement? *Better Homes and Gardens, 24:* 40, 1946.

GLYCOGEN IN BRAIN—The Effect of Hypoglycemia and Age on the Glycogen Content of the Various Parts of the Feline Central Nervous System. Shirley Farris and Harold E. Himwick. *American Journal of Physiology, 146:* 389–393, 1946.

GRANDMOTHERS—The Sociological Function of the Grandmother. Hans Von Hentig. *Social Forces, 24:* 389–392, 1946.

GUMPERT, M.—What Is the Natural Lifespan? *Saturday Review of Literature, 29:* 15, 1946.

HEART DISEASE—Encouraging Trends in Heart Disease. *Statistical Bulletin, Metropolitan Life Insurance Co., 27:* 6–8, 1946.

HIMWICK, HAROLD E.—(See Farris, Shirley, and Harold E. Himwick.)

HINDS, EWART G.—(See Stern, Karl, Ewart G. Hinds, and Brigette A. Askonas.)

HORMONES—The Effects of Sex Hormones on the Copulatory Behaviour of Senile White Rats. R. S. Minnick, C. J. Warden, and S. Arieti. *Science, 103:* 749–750, 1946.

KEMP, M. W.—Conflicts and Psychogenic Maladjustments Incidental to Age. *Minnesota Medicine, 28:* 715–717, 1945.

LADER, LAURENCE—One Way to Live Longer. *Coronet, 20:* 36, 1946.

LAWTON, GEORGE—So You Want to Live Long. *Ladies' Home Journal, 63:* 202, 1946.

LIPETZ, BASILE—(See Feldman, Capt. Fred, Lt. Samuel Susselman, Basile Lipetz, and S. Eugene Barrera.)

LONGEVITY—Longevity at a Record High. *Statistical Bulletin, Metropolitan Life Insurance Co., 27:* 1–3, 1946.

MAINER, R. H.—Are Private Pensions Justified? *Canadian Forum, 26:* 81, 1946.

MCCULLAGH, E. PERRY—Climacteric—Male and Female. *Cleveland Clinic Quarterly, 13:* 166–176, 1946.

MINNICK, R. S.—C. J. Warden, and S. Arieti. The Effects of Sex Hormones on the Copulatory Behavior of Senile White Rats. *Science, 103:* 749–750, 1946.

NUTRITION—Nutrition in the Aged. *Nutrition Reviews, 4:* 172–173, 1946.

PENSIONS—Are Private Pensions Justified? R. H. Mainer. *Canadian Forum, 26:* 81, 1946.

Old Age Pension. B. A. Scovil. *Canadian Forum, 26:* 91, 1946.

PNEUMONIA—Pneumonia in the Aged. F. D. Zeman and K. Wallach. *Archives of Internal Medicine, 77:* 678–699, 1946.

PSYCHIATRY—A Gerontological Treatise of the Renaissance. Karl Stern and Thomas Cassirer. *American Journal of Psychiatry, 102:* 770–773, 1946.

Ageing and Detoxification Studies in Hippuric Acid Synthesis During Psychoses of the Involutional and Old Age Group. Karl Stern, Ewart G. Hinds, and Brigette A. Askonas. *American Journal of Psychiatry, 102:* 325–329, 1946.

Conflicts and Psychogenic Maladjustments Incidental to Age. M. W. Kemp. *Minnesota Medicine, 28:* 715–717, 1945.

Electric Shock Therapy of Elderly Patients. Capt. Fred Feldman, Lt. Samuel Susselman, Basile Lipetz, and S. Eugene Barrera. *Archives of Neurology and Psychiatry, 56:* 158–170, 1946.

O'NEILL, J. J.—You're as Old as Your Veins. *Science Digest, 20:* 1–3, 1946.

RAPP, SAHRA S.—Boarding Care for the Aged Sick. *The Family, 27:* 192–196, 1946.

RATCLIFF, J. D.—Can Science Double Your Life? *Everybody's Digest,* July, 1946.

RENAISSANCE—A Gerontological Treatise of the Renaissance. Karl Stern and

Thomas Cassirer. *American Journal of Psychiatry, 102:* 770–773, 1946.

RETIREMENT—Why not Rehearse Your Retirement? R. Giles. *Better Homes and Gardens, 24:* 40, 1946.

RICHTER, C. P.—(See Dieke, S. H., and C. P. Richter.)

ROGERS, HELEN C.—A Librarian's Working Knowledge of the Aged. *Special Libraries, 37:* 183–188, 1946.

SCOVIL, B. A.—Old Age Pension. *Canadian Forum, 26:* 91, 1946.

SOCIAL SECURITY—More Pay for the Aged? Relief vs. Insurance. *U. S. News, 21:* 42–43, 1946.

SPLEEN—Age Changes in the Vascular Architecture and Cell Content in the Spleens of 100 Wistar Institute Rats, Including Comparisons with Human Material. Warren Andrew. *American Journal of Anatomy, 79:* 1–73, 1946.

STERN, KARL—Ewart G. Hinds, and Brigette A. Askonas. Ageing and Detoxification Studies in Hippuric Acid Synthesis During Psychoses of the Involutional and Old Age Group. *American Journal of Psychiatry, 102:* 325–329, 1946.

—and Thomas Cassirer. A Gerontological Treatise of the Renaissance. *American Journal of Psychiatry, 102:* 770–773, 1946.

SUSSELMAN, LT. SAMUEL—(See Feldman, Capt. Fred, Lt. Samuel Susselman, Basile Lipetz, and S. Eugene Barrera.)

TOXICITY OF THIOUREA—Age and Species Variation in the Acute Toxicity of Alpha-Naphthyl Thiourea. S. H. Dieke and C. P. Richter. *Proceedings of the Society for Experimental Biology and and Medicine, 62:* 22–25, 1946.

VEINS—You're as Old as Your Veins. J. J. O'Neill. *Science Digest, 20:* 1–3, 1946.

VON HENTIG, HANS—The Sociological Function of the Grandmother. *Social Forces, 24:* 389–392, 1946.

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WARREN, MARJORY W.—Care of the Chronic Aged Sick. *The Lancet, i:* 841–843, 1946.

ZEMAN, F. D.—and K. Wallach. Pneumonia in the Aged. *Archives of Internal Medicine, 77:* 678–699, 1946.

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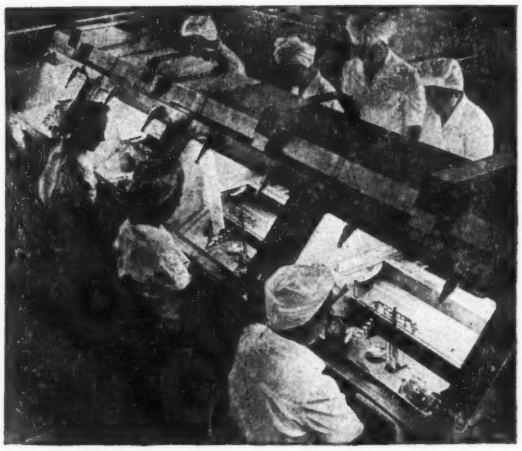

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spray dried whole milk skim milk dried brewer's yeast (source of B vitamins) fortified with riboflavin concentrate vitamin A and D concentrate from fish liver oil irradiated ergosterol (vitamin D) ascorbic acid vitamin C niacinamide monosodium phosphate and iron citrate
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Gerilac—A DIETARY SUPPLEMENT FOR THE AGED. Gerilac contains spray-dried whole milk and skim milk and is fortified with vitamins A and D, B complex, C, together with niacinamide, monosodium phosphate and iron citrate. Available at pharmacies in 1-lb. tins.
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